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EDITORIAL

Cardiac Arrhythmias Complicating Surgery

THE PAST DECADE has witnessed a very exciting upsurge of interest in the recognition and treatment of cardiac arrhythmias. In part this has been brought about by improved methods of recognizing the arrhythmias and by an increasing understanding of the pathophysiology with which they are associated. Interest also has been stimulated by the cardiac surgeon, who in his manipulation within and about the heart has obtained information about arrhythmias and the methods by which they may be corrected.

Let us restate certain concepts and principles concerning the pathophysiologic conditions which may be precipitated by abnormal rhythms. Either tachycardia, bradycardia, or a normal rate may result from an arrhythmia. Initially, tachycardia is beneficial because it increases the minute volume output of the heart. This effect probably persists until the rate is 140 to 160 per minute. Thereafter an interference with early diastolic filling of the heart develops and minute volume output falls. This may be accompanied by a serious impairment of coronary circulation and a series of adverse metabolic changes which contribute to the loss of kinetic energy. The abnormal physiology which results from bradycardia stems from the fact that each ventricular chamber is capable of increasing its stroke volume only to a limited degree. Since the minute volume of the heart cannot be increased when the rate falls, bradycardia favors the development of congestive failure.

GENERAL CONSIDERATIONS IN TREATMENT

The incidence of arrhythmias in general surgery is small as compared to cardiac surgery. The reasons are quite evident. It is unusual to operate in face of cardiac disease in general surgery. In cardiac surgery the heart uniformly is organically and functionally abnormal.

It is essential that a competent analysis of cardiac function be completed prior to operative interference. This review may alert the physician to the likelihood of arrhythmias and to the probable functional response should unusual cardiac action develop.

The useful drugs in the treatment of abnormal rhythms may be divided into three classes: The first has a specific effect upon the myocardium and includes digitalis, quinidine, and procaine. The second influences the sympathetic or parasympathetic nervous system. Adrenalin, atropine, and acetylcholine are examples of these drugs. The third category alters the action potential system by influencing metabolic processes. This includes potassium and magnesium.

It is essential to understand before the time of surgery what cardiac drugs have been prescribed. This is particularly pertinent in regard to digitalis, which may of itself initiate significant arrhythmias.

A final consideration in the general approach to the treatment of cardiac arrhythmias concerns the obvious fact that the opportunity for oral medications immediately prior to or following surgery is quite limited. Most abnormal

rhythms during surgery are treated with intravenous medication. Cardiac medications applied in this fashion are potentially dangerous, and their dosage must be carefully adjusted. Multiple drugs generally should not be used in this fashion. When one medication can satisfy a discreet purpose it should be used alone.

Treatment of Specific Arrhythmias

1. *Sinus tachycardia* is an ordinary expected response to the stress of surgery. It may be precipitated by various events in addition to the stress, including blood loss. Under such circumstances, sinus tachycardia rarely requires specific cardiac medication. If it does, 0.5 mg neostigmine intravenously is generally effective.

2. *Premature systoles*, although generally benign, may be the forerunner of paroxysmal atrial tachycardia, atrial fibrillation, or ventricular tachycardia.

As mentioned previously, the choice of drugs is limited to those agents which may be given safely intravenously. Currently, Xylocaine in a concentration of 1 mg per 2 to 3 pounds of body weight has proved very effective in the treatment of atrial and ventricular premature systoles. Xylocaine is a local anesthetic which, in contrast to procaine or procaine amide, has little hypotensive effect. It is less toxic than any intravenous preparation of quinidine.

On those occasions when multiple premature atrial contractions cannot be controlled by Xylocaine, the remaining effective drug is a digitalis glycoside.

3. *Paroxysmal supraventricular tachycardia* in the absence of previous digitalis administration is best treated by full digitalization. Cedilanid (lanatoside C) is preferable because of its rapid action and elimination.

Xylocaine in the doses previously described has been observed to be effective in this type of arrhythmia. Because it is rapidly eliminated the medication may have to be repeated within 10 or 20 minutes. Xylocaine is apparently more effective than Pronestyl (procaine amide). Occasionally when supraventricular tachycardia has not responded to either digitalis, Xylocaine, or Pronestyl, it may be converted to normal sinus rhythm by the use of Neo-synephrine hydrochloride. This medication is used in a 1 per cent solution intravenously, and approximately 1 mg is generally effective in terminating the abnormal rhythm. The drug is contraindicated in patients with severe hypertension and advanced coronary artery disease.

When paroxysmal supraventricular tachycardia has been initiated by digitalis intoxication the treatment of choice is potassium chloride. This drug is available for intravenous use in ampuls containing 3.7 Gm or 50 meq. The contents are usually dissolved in 500 cc of 5 per cent glucose in distilled water and administered by intravenous drip.

4. *Paroxysmal atrial fibrillation* is the most frequent arrhythmia to develop in the course of surgical procedures. Paroxysmal atrial flutter is much less common.

The treatment of choice is digitalization intravenously if the drug has not been previously administered. In patients already digitalized additional doses may be given with caution. No purpose is served in attempting to revert this rhythm to a normal sinus mechanism through the use of quinidine gluconate. Even in those circumstances in which normal sinus rhythm does not develop following digitalization the drug accomplishes a most beneficial effect by controlling the ventricular response and thereby minimizing the degree of pathophysiology.

5. *Paroxysmal ventricular tachycardia* is an important and often lethal arrhythmia which arises frequently during the course of aortic valve surgery performed by the closed methods. It is not encountered frequently in general surgery except as a complication of the induction of anesthesia. In the latter circumstances ventricular fibrillation and cardiac arrest are much more common.

In our experience the most effective drug for intravenous use is Xylocaine in the same doses already described. Quinidine and procaine amide are effective medications when administered intravenously. The former is obtainable as a gluconate solution. The usual dose of 0.5 Gm is administered by diluting the quinidine gluconate in 50 to 150 cc of 5 per cent glucose in water. This solution is administered no more rapidly than 2 to 3 cc per minute. The usual recommended dose of

procaine amide is approximately 100 mg per 5 minutes, with an absolute maximum of 1 Gm.

Constant electrocardiographic observations and blood pressure determinations are required when either quinidine or procaine is being used intravenously.

6. *Cardiac arrest* is a true catastrophe. In our experience it occurred in 12 of 1,500 patients subjected to mitral commissurotomy. Four of these subsequently died. *Ventricular fibrillation* occurred 21 times during the course of the same number of mitral commissurotomies. Of these, 50 per cent were fatal. Of those who survived an additional 50 per cent died thereafter. Our ability to salvage these cases is, therefore, small. The techniques advised for resuscitation are cardiac massage and electrical stimulation or a combination of both. It is unusual that these procedures can be augmented or improved upon by any particular drug.

The application of local anesthetics to the surface of the heart in the course of cardiac surgery to prevent any and all of these complications is routine. The effectiveness of these drugs by intravenous drip is at best questionable.

In summary, the treatment of cardiac arrhythmias complicating surgery is based upon the identical principles which govern the therapy under more ordinary circumstances. The only modifications are dictated by the need to rely upon intravenous medications and the requirement to control the abnormal physiology as quickly as possible. The entire issue always is seriously complicated by the presence of organic cardiac disease.

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Clinical Studies

The Work Electrocardiogram

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THE work-electrocardiogram test in common use, the Master two-step test[1] or one of its modifications, is essentially a qualitative test in that it is scored "positive" or "negative." A positive result is regarded as indicating the development of acute myocardial ischemia under stress and implying a pathologic degree of narrowing of the coronary arteries. A negative result is regarded as excluding these possibilities.[2] The test is relatively easy to carry out and, on the basis of probability, is valid.[2,3]

On a priori grounds it is difficult to believe that the two-step test separates, by a simple dichotomy, all of those "with" from all of those "without" a pathologically important degree of "coronary narrowing." Moreover, were such a separation possible, it is reasonable to believe that there must exist varying degrees of coronary sufficiency or insufficiency in both groups. The concept of positive or negative tends to prevent the full exploitation of the work electrocardiogram. As an alternative, it is suggested that the work electrocardiogram should be subjected to the same intensive and extensive study which the rest electrocardiogram has received. None of the findings should be rejected as insignificant until follow-up studies have proven that they have no value, on the basis of probability, in contributing to the diagnosis of coronary heart disease or, where present, its degree of severity.

The main purpose in reporting our experience with the work electrocardiogram is to emphasize the value of a wide range of work loads in carrying out the test. If the results of the initial test revealed good evidence of acute myocardial ischemia, the amount of exercise was reduced until such evidence was no longer present. If the initial result was inconclusive, the work load was increased gradually until either good evidence of myocardial ischemia was obtained or a satisfactory degree of exercise tolerance was demonstrated. This "individualization" of the test was costly in time and effort, but considered to be justified in selected cases. Nearly all of our subjects were men on active duty in the military service, and since frequently the man's career was at stake, a definite decision had to be reached if at all possible.

PROCEDURE

In performing exercise tests, we used a motor-driven treadmill, Master's single or double two-step test, and a modification[4] of the Harvard step-test.[5] The latter consists of a single step platform, behind and above which are a series of horizontal rods providing hand holds at a convenient height for any subject (Fig. 1). The rate of work can be varied either by the number of step-ups per minute or by adjusting the height of the step. For a given rate and height of step, the amount of work depends on the duration. Unless otherwise indicated, we used a step 20 in. high and a step-up every 3 sec. The hardest grade of work used was a step-up every 2 sec for 5 min. Only persons

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in good training can complete this test. The information obtained in interviewing the subject usually sufficed to determine the amount of exercise to use in the initial test. The response to the first test was useful in estimating the level of work for the subsequent test. The more the work load exceeded the customary level for the subject, the greater the caution that was exercised.

Useful information was sometimes obtained from additional tests. These included the administration of 100 per cent oxygen, potassium chloride, glucose, and the effect of hyperventilation. Levy's anoxia test was used occasionally.[6]

The findings in the work electrocardiograms were compared with the control one. The principal items requiring evaluation were changes in the RS-T segment, RS-T junction, the T waves, and changes in conduction. A distinction was made among three types of changes in the RS-T segment: (1) the flat downward displacement of the whole ST segment, (2) the downward scalloping resembling the change due to digitalis, and (3) the straight downward sloping RS-T segment similar to that seen in left ventricular strain. Accurate measurement of displacement is sometimes difficult because of the wandering of the baseline, poor definition of onset or offset of QRS, and the influence of the auricular T waves.[7] Every "abnormality" was regarded as a challenge, as to its possible pathologic significance. All extenuating factors were considered, such as an unusually high heart rate, the presence of hypertension, the change in position of the heart and electrical axes, and the possibility of reproducing the "abnormalities" by means other than exercise.

Case Material

Of the 14 cases to be presented only the first six patients were known to have coronary heart disease on the basis of findings other than those from the work electrocardiogram. These 14 were selected from a total of 136 patients referred to the cardiovascular clinic, at the U. S. Naval School of Aviation Medicine, for evaluation with regard to coronary heart disease and on whom work electrocardiograms were obtained. It should be mentioned that our experience includes tests on upwards of 400 subjects which were carried out either as a matter of routine or for other reasons.

Fig. 1. The single step with hand grips. The height of the step is adjustable.

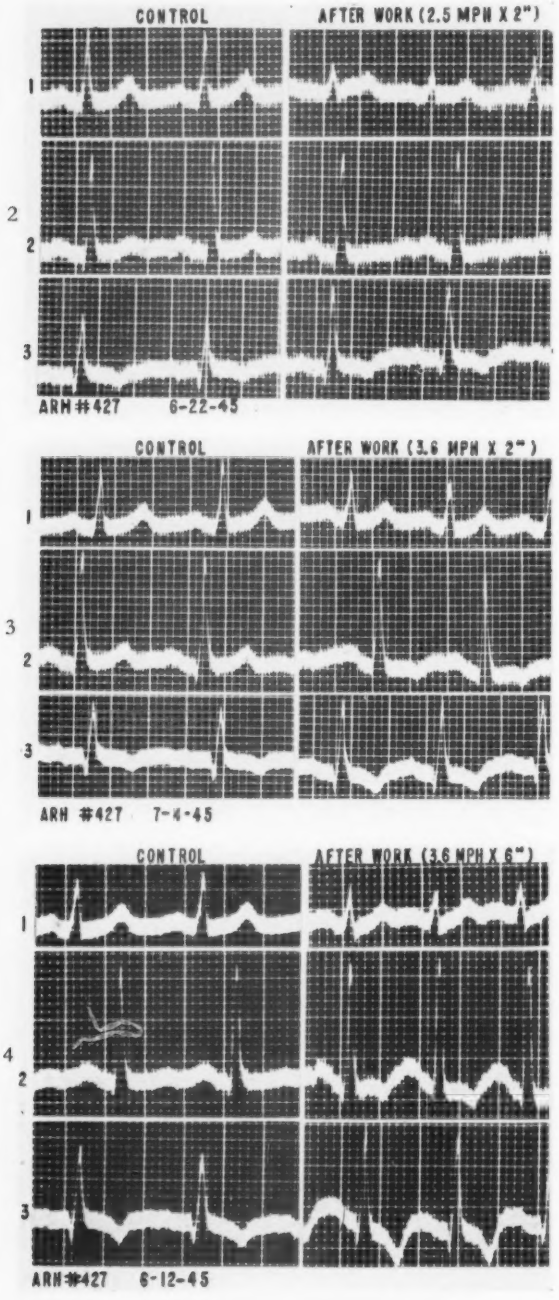
Case Histories

CORONARY ARTERY DISEASE WITH GREATLY REDUCED RESERVE

Case 1. An officer on active duty in the U. S. Navy, 38 years of age, was referred for evaluation because, during a routine examination, he was discovered to have slight elevation of the blood pressure and a murmur in the mitral area. He had no complaints of any kind. His duties were those of an engineer, and there was little or no exercise associated with his work. Examination revealed an apparently healthy person 74 in. tall, weighing 270 lb. The heart was not enlarged, the rhythm was regular, and a grade 2 systolic murmur was heard over the precordium. The blood pressure was 140/100. There were no congestive phenomena. Radiogram of the thorax revealed no abnormality, and the heart was normal in size and shape. The electrocardiogram was

normal except for marked widening of the QRS-T angle with flat T waves in lead 2 and inverted T waves in lead 3. A diagnosis was made of slight hypertension and possible coronary heart disease, and re-evaluation was requested.

Prior to his discharge from the service 15 months later he was seen on numerous occasions, and a series of tests was carried out. The effect of progressive increments of exercise is shown in the electrocardiograms in Figures 2 3, and 4. It is seen that as the work load was gradually increased, progressively greater alterations occurred in the T waves, finally resulting in definite inversion of the T waves in lead 2. In addition, it can be seen that the initially abnormal QRS-T angle of 80 degrees in the control tracings increased with each work load to 110 degrees, 125 degrees, and finally to 140 degrees. Since the QRS axis changed no more than 15 degrees, this increment in the QRS-T angle represents a primary T wave change.



Figs. 2, 3, and 4. Electrocardiograms in case 1 showing effect of progressive increments of exercise.

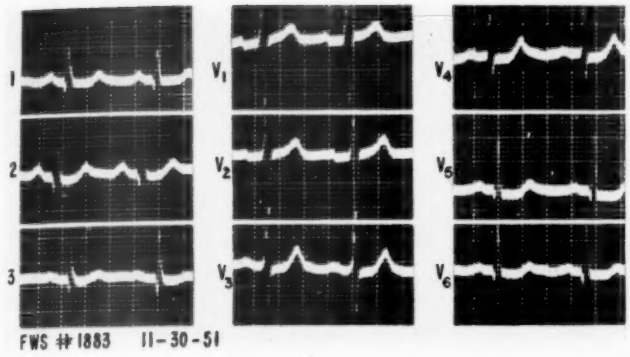
On five occasions he was exposed progressively to smaller amounts of oxygen in the inspired air beginning at 16 per cent for a short period, and concluding at 10.47 per cent for 15 min. Only slight alterations were observed. On two occasions he was exercised while breathing 100 per cent oxygen; no significant T wave changes were observed at 2.5 miles/hour for 2 min, but slight change occurred at 3.6 miles/hour for 6 min.

A definite diagnosis was made of slight hypertension and coronary heart disease with greatly reduced functional reserve. A year and one-half following his discharge and during the course of litigation concerning his cardiovascular disability, he died rather suddenly. Autopsy revealed acute coronary occlusion and widespread disease of the coronary arteries.

CORONARY HEART DISEASE WITH GREATLY REDUCED RESERVE

CASE 2. A retired chief boatswain's mate, 47 years of age, was referred for evaluation with a tentative diagnosis of angina pectoris. Following retirement, he obtained work in the fire department. He had always been well and strong until a year previously when he first noted an unusual degree of dyspnea on exercise. During the preceding four weeks he had noted that emotional upsets sometimes produced a feeling of pressure in the chest with pain radiating down the left arm and numbness of the left hand. One week previously, while practicing ladder drill, he had developed severe pain in the chest and shortness of breath on carrying a person on his back up a ladder. The symptoms quickly disappeared on resting. There were no other complaints. Physical examination revealed a hypersthenic person 65 in. tall and weighing 198 lb. The heart was not enlarged, the rhythm was regular, and no murmurs were heard. The blood pressure was 142/102. There were no congestive phenomena. Radiogram of the chest revealed the heart to be at the upper limit of normal in size.

The electrocardiograms obtained before and after exercise are shown in Figures 5 and 6. In the tracing taken at rest, there is slight downward displacement and sagging of the ST segments in significant leads. After exercise, 25 step-ups in 1 min, there is marked downward displacement of the RS-T segments in several significant leads without appreciable change in the T axis. This rather mild exercise did not produce pain in the chest, and the increase in heart rate was small. A diagnosis



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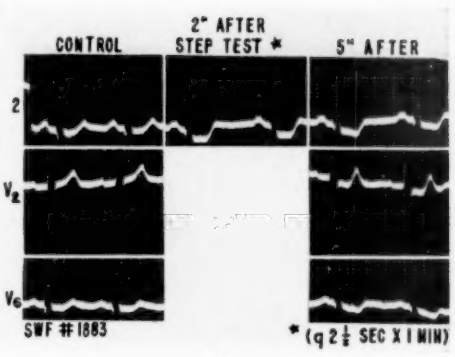

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Fig. 5. Case 2. Resting electrocardiogram suggesting myocardial ischemia. Fig. 6. Electrocardiograms before and after exercise consisting of 25 step-ups in one minute. Increased ST changes confirmed myocardial ischemia.

was made of hypertensive and coronary heart disease with greatly decreased reserve.

HYPERTENSION AND CORONARY INSUFFICIENCY

CASE 3. An officer in the U. S. Navy, 46 years of age, had always been well and strong until five years previously when he was discovered to have hypertension. He remained asymptomatic until two months previous when he first noted pain in the chest and arms coming on with exertion, lasting 2 to 5 min, and relieved with rest. Physical examination revealed a healthy appearing person 72 in. tall, weighing 185 lb. The heart was not enlarged, the sounds were of good quality, and the blood pressure was 160/100. There were no congestive phenomena, and there were no significant vascular changes in the ocular fundi. The radiogram of the chest was normal except for slight prominence of the left ventricle, but the heart measurements fell within the normal range. The electrocardiogram was normal except for rather low T waves in lead 2 and leads V_5 and V_6. He was placed on a strict regimen including a low-fat diet, vasodepressor drugs, and reduced activity. His blood pressure gradually returned to normal, and the frequency of his anginal attacks greatly diminished.

Re-examination four years later revealed no significant change except that the blood pressure was 130/84. The electrocardiograms obtained at rest and following a single Master test are shown in Figure 7. The control tracing at this time showed marked improvement in the amplitude of the T waves in both the limb and left precordial leads and would undoubtedly be considered normal. However, after light exercise, the marked downward displacement of the RS-T segment in V_5 with a slow return to the initial configuration clearly demonstrated coronary insufficiency. Two years later, when last examined, he was able to carry out light activities and rarely experienced anginal attacks.

PROVED CORONARY ARTERY DISEASE WITH ATYPICAL SYMPTOMS

CASE 4. A U. S. Naval "Chief," 41 years of age, was referred for cardiac evaluation. He had always been well and strong until four years previously when he gradually became aware of epigastric distress. These episodes increased in frequency and severity but were always confined to the epigastric and lower substernal areas. Various types of distress were reported, the most significant of which was slight substernal pain sometimes associated with numbness of the fingers. Such attacks were not related to exertion, and the examiner did not think they were due to myocardial ischemia. An electrocardiogram taken four years previously had been reported as showing "heart strain." Physical examination revealed a healthy appearing person 68 in. tall, weighing 160 lb. The heart was not enlarged, the sounds were of good quality, and no murmurs were heard. The blood pressure was 130/80. Radiogram of the chest revealed no abnormality of the heart or lungs, and the electrocardiogram was considered to be within normal limits.

A further evaluation was carried out three weeks later. Electrocardiograms obtained at rest and following a double Master and our step test are shown in Figures 8 and 9. Following the Master test there was downward displacement of the RS-T junction in lead 2. Following the hard work test, in addition to downward displacement of RS-T, there was a decrease in the amplitude of the T waves in lead 1 and in V_5 and V_6 which persisted

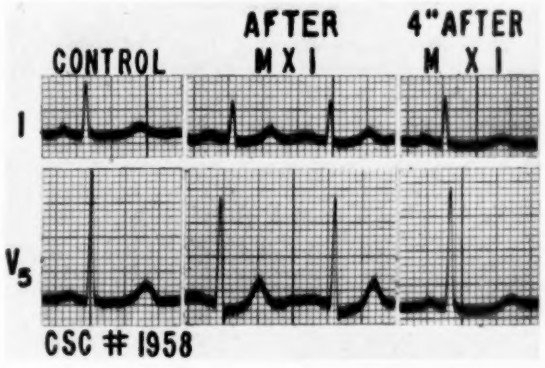
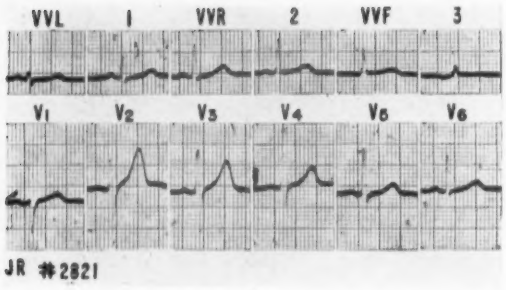


Fig. 7. Case 3. Electrocardiograms after single Master test suggesting coronary insufficiency.



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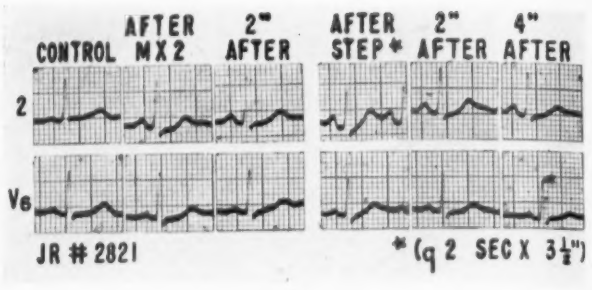

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Fig. 8. Case 4. Electrocardiogram under resting conditions. The limb leads are "equated" and the right arm lead (VVR) is "upright." Fig. 9. Electrocardiograms after Master test and a hard work test.

for at least 6 min. Unlike case 1 the QRS-T angle in the frontal plane diminished with exercise due to a vertical shift of the T vector from plus 30 degrees to plus 50 degrees. In the horizontal plane, however, the QRS-T angle increased as a result of the anterior rotation of the T axis. Hyperventilation caused a slight but definite decrease in the amplitude of the T waves, particularly in lead 1 but also in leads 2 and V_5. There was no significant change in the electrocardiogram following the administration of 100 per cent oxygen for 30 min.

A diagnosis of coronary heart disease was made very largely on the basis of the changes in the work electrocardiogram. There was no significant change in symptomatology until five months later when he was awakened during the night with severe substernal pain with radiation to the neck, shoulders, and arm on the left side. An electrocardiogram obtained at the time of his admission was characteristic of acute myocardial infarction involving the anterior wall of the heart. The next morning while he was being examined, his respirations suddenly became irregular and a pulse could not be obtained. Attempts at resuscitation were unavailing. The autopsy revealed atherosclerosis 2 cm below the origin of the anterior descending branch of the left coronary artery, at which point there was almost complete occlusion of the vessel. A thorough search revealed no atherosclerotic changes in the other coronary vessels. The case was regarded as unusual in showing such a limited involvement of the coronary tree.

NEUROCIRCULATORY ASTHENIA VS. CORONARY DISEASE

Case 5. This 24-year-old male had always been well and strong until two and one-half years previously when, while in the Army, he suddenly became weak and dizzy. He was hospitalized for a period of 10 months, then given a medical discharge with a diagnosis of nervousness and heart trouble. He continued in fair health until seven months prior to admission when he began to complain of precordial pain occasionally accompanied by pain in the left shoulder and elbow. The pain was present on and off during the day but was not related to exertion. He denied dyspnea, palpitation, or any other symptoms. On physical examination, he appeared ill. He was 75 in. tall and weighed 176 lb. The heart was not enlarged, the

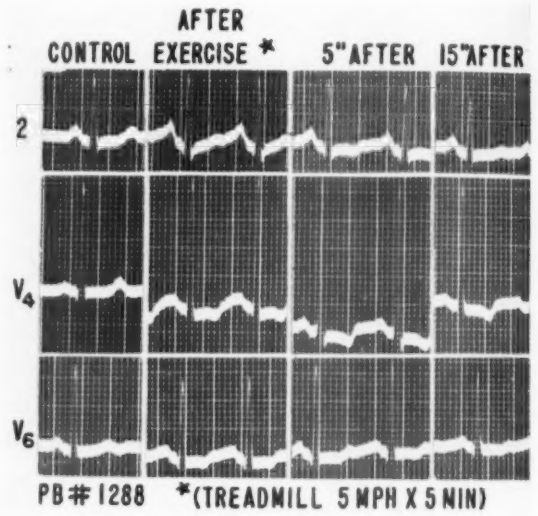


Fig. 10. Case 5. Electrocardiograms after exercise on treadmill for 5 min at 5 miles/hr. The changes indicate myocardial ischemia.

rhythm was regular, and no murmurs were heard. The blood pressure was 160/90. Examination of the ocular fundi revealed no abnormalities of the vessels. There were no congestive phenomena. The electrocardiogram at that time revealed frequent ventricular premature beats, and the T waves were abnormally low in V_3 through V_6. A diagnosis was made of neurocirculatory asthenia, irritable heart, and possibly coronary heart disease.

He was re-examined one year later. He still complained of vague chest and left shoulder pain but, by his description, the pain was not suggestive of myocardial ischemia. The blood pressure was 140/98, and no changes were noted on physical examination. A comparison of the radiograms of the chest, however, revealed a probably increased heart size during the interval. There was marked calcification in the aortic arch and the costal cartilages. Levy's anoxia test was positive. Electrocardiograms taken at rest and after exercise on the treadmill for 5 min at 5 miles/hour are shown

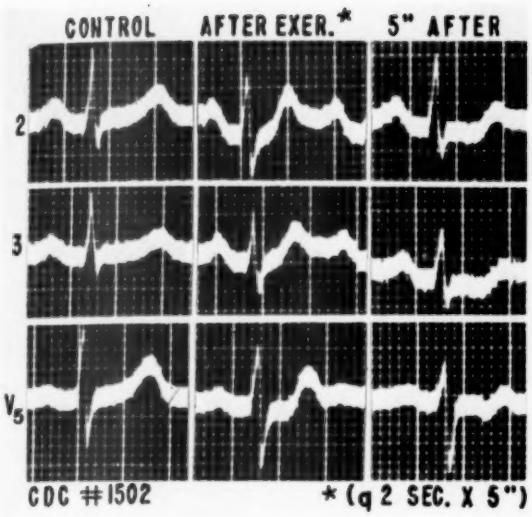


Fig. 11. Case 6. Electrocardiograms after exercise on 20-in. step. There is evidence of myocardial ischemia.

in Figure 10. Immediately following the exercise, the patient was given 100 per cent oxygen to breathe. The downward displacement of the RS-T segments and the inversion of the T waves clearly indicated myocardial ischemia. A definite diagnosis was made of coronary heart disease with moderately decreased functional reserve.

CORONARY ARTERY DISEASE WITH CHANGING LEVELS OF CARDIAC RESERVE

CASE 6. An officer in the U. S. Navy, 44 years of age, was well and strong until 13 months previously when, three days after a period of strenuous physical effort, he developed the typical symptomatology of the intermediate coronary syndrome. At first his exercise tolerance was greatly reduced, and nitroglycerin was required for the relief of anginal attacks. Gradually, his exercise tolerance increased, and for the past six months he had been asymptomatic. Physical examination at that time revealed a healthy appearing person 70 in. in height, weighing 176 lb. The heart was not enlarged, the sounds were of good quality, and no murmurs were heard. The blood pressure was 154/96. There were no congestive phenomena, and the radiogram of the chest revealed no abnormality.

The resting electrocardiogram was normal. The anoxia test, breathing 10 per cent oxygen for 20 min, revealed only slight lowering of the T waves. Electrocardiograms obtained during full inspiration and full expiration revealed very slight alterations from the control record. After 3 min of strenuous exercise, one 20 in. step every 2 sec, moderate changes in leads 2, 3, and V_6 appeared; the RS-T junction was displaced downward less than 0.5 mm. The T waves were reduced in amplitude in leads 2, 3, and V_6. He was seen for re-evaluation a year later during which period he had had no cardiovascular symptoms. At that time he weighed 169 lb, and his blood pressure was 126/78. The resting electrocardiogram and the electrocardiograms taken after five minutes on the 20-in. step, one step every 2 sec, are shown in Figure 11. Although the results of the exercise test indicated some degree of acute myocardial ischemia, it was concluded that his cardiovascular reserve was excellent inasmuch as he was able to continue hard work for a period of five minutes.

Re-examination nearly eight years later disclosed that during the interval he had had no symptoms referable to the cardiovascular system except slight shortness of breath on climbing stairs. He had not followed his diet and had gained over 15 lb in weight. The heart was not enlarged, and there were no murmurs. The blood pressure was 160/104. The blood cholesterol level was 323 mg per cent, and the atherogenic index 118. Electrocardiograms were obtained at rest and following a 3-sec step test for 69 sec. The RS-T segments were downwardly displaced in leads 2 and V_5. There was downward displacement greater than 0.5 mm in leads 2 and V_6. Although his functional reserve was small, he continues to this time, nine and one-half years later, to carry out light duties without any symptoms.

POSSIBLE CORONARY HEART DISEASE

CASE 7. A U. S. Navy officer, 37 years of age, was referred for evaluation with a diagnosis of possible coronary heart disease. He had always been unusually strong and well until two years previously when he noticed difficulty in breathing and easy fatigability. He complained not only of dyspnea on exercise but also of "difficulty in getting sufficient air" even at rest. For over a year he had noticed a tight feeling under the sternum and constriction in the throat when he became emotionally upset, and sometimes when eating. This distress never lasted over 2 to 3 min and was relieved by lying down. He associated these attacks with epigastric discomfort and not with exercise. He was 73 in. tall and weighed 180 lb. Physical examination revealed no definite abnormality. The heart was not enlarged, the rhythm was regular, and no murmurs were heard. The blood pressure was 120/78. Routine laboratory examinations revealed no ab-

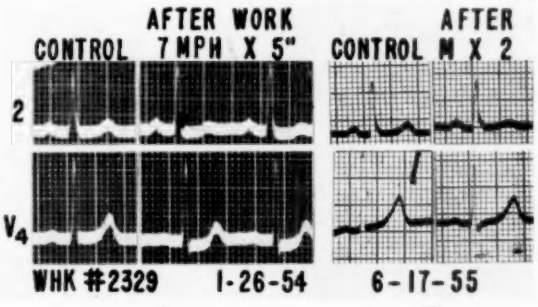


Fig. 12. Case 7. Electrocardiograms after exercise, walking on treadmill for 5 min at 7 miles/hr. Repeat test after strenuous single step test.

normality, and the basal metabolic rate on two occasions was −10 per cent and −16 per cent.

The electrocardiogram obtained at rest was normal except for rather low T waves in the limb leads. Following forced hyperventilation, the T waves in the limb leads became flat, but there was no alteration in the RS-T segments. An electrocardiogram obtained immediately after walking on the treadmill for five minutes at seven miles an hour (Fig. 12A) showed lowering of the T waves, scalloping of the RS-T segment in lead 2, and downward displacement of the RS-T segments in lead V_4. On another occasion, he was subjected to strenuous exercise using the single step with similar results.

It was our opinion that this officer had symptoms of psychosomatic origin but that he probably had some coronary insufficiency. During a follow-up study, carried out in a hospital five months later, a double Master test was performed (Fig. 12B). The only change after exercise was slight lowering of the T waves in the limb leads. More information would have been obtained and possibly a definitive diagnosis could have been established if more strenuous exercise had been employed.

ATYPICAL CHEST PAIN DUE TO CORONARY INSUFFICIENCY

CASE 8. A U. S. Naval officer, 37 years of age, was referred for evaluation of chest pain. He had been in his usual state of good health until a year previously when he first noted pain in the chest with radiation to the left arm. He did not relate the onset of the pain to exercise or excitement, and it never had awakened him at night. He did suffer many attacks, however, at unexplained times during the day. The pain always began severely, gradually tapered off, and never lasted more than a minute. In addition to the pain, he also noted shortness of breath on exercise, and on several occasions he was awakened at night with shortness of breath. Physical examination revealed a person with florid complexion, 70 in. tall, weighing 165 lb. The heart was not enlarged, the rhythm was regular, and no murmurs were heard. The blood pressure was 162/94. There were no signs of congestive failure. Radiogram of the chest revealed a normal cardiac contour and clear lung fields. Barium studies of the esophagus and stomach were negative. The blood serum cholesterol was 378 mg per cent, and the atherogenic index was 79. The ballistocardiogram was within normal limits.

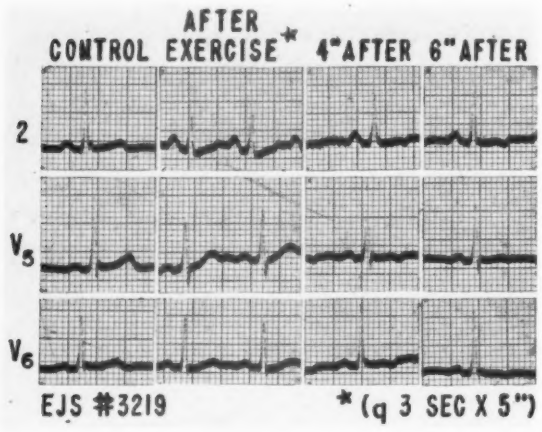


Fig. 13. Case 8. Electrocardiograms after exercise (single step test).

The electrocardiogram obtained at rest revealed rather low T waves in leads 2 and V_6 but otherwise was within normal limits. Electrocardiograms obtained after exercise for 5 min at a rate of one step-up every 3 sec are shown in Figure 13. The principal abnormality was lowering of the T waves in leads 1 and V_4 and slight inversion of the T waves in leads 2, 3, V_5 and V_6. The T waves had not returned to normal at the end of 10 min. The RS-T displacement was minimal. The T vector changes were quite similar to those in case 1. The QRS-T angle in both the frontal and horizontal planes widened due to an anterior and superior spatial rotation of the T vector. This would suggest that the area of ischemia lay in the posterolateral wall of the left ventricle.

A diagnosis was made of coronary heart disease, angina pectoris, slight hypertension and hypercholesterolemia. Because of the atypical history and the fact that the only positive objective findings were the electrocardiographic alterations, an attempt was made to determine whether these changes occurred after very light exercise. The results are shown in Figure 14 for both short exercise at a high work load, namely, 15 step-ups in 30 sec, and for a conventional single Master test. In both instances the changes should be regarded as significant. This finding

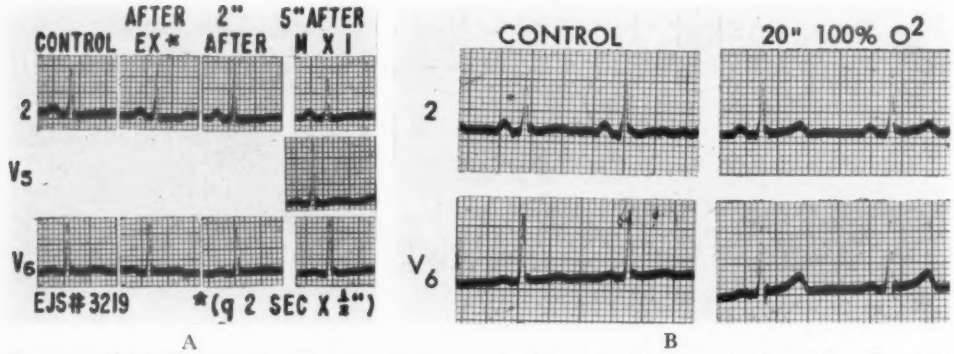
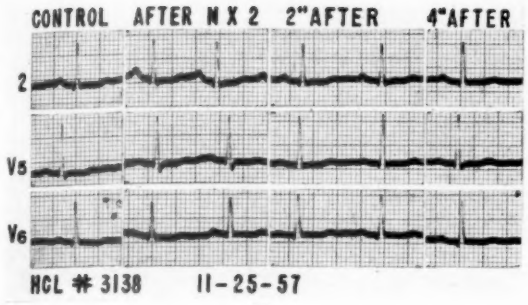


Fig. 14A and 14B. Case 8. Electrocardiograms after increasing increments of exercise. See text.



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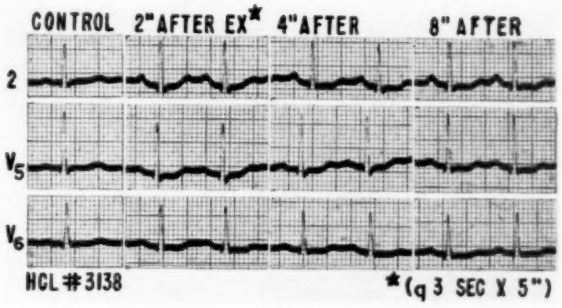

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Figs. 15 and 16. Case 9. Electrocardiograms after Master two-step test and 5 min single step test.

indicates a very small coronary reserve. The patient noted slight pain at the end of the single Master step test but none during the short bout of exercise on the 20-in. step. Following the administration of 100 per cent oxygen for 20 min, the T waves became upright in leads 2 and V_6 (Fig. 14B).

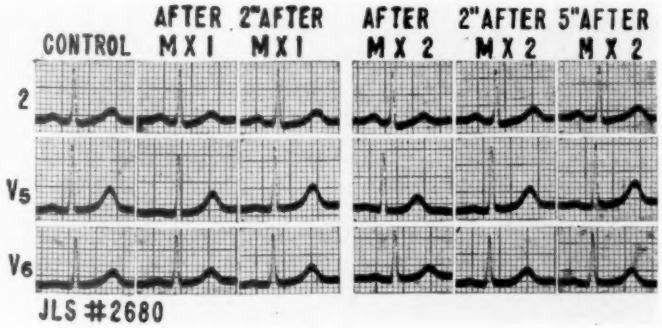
ASYMPTOMATIC PATIENT WITH ABNORMAL T WAVES

CASE 9. A 47-year-old chief petty officer was referred for evaluation because of electrocardiographic abnormalities found during a routine physical examination. He was completely asymptomatic, and the only item of possible significance in his past medical history was the fact that 20 years previously he was hospitalized for one week with "left sided pleurisy." Physical examination revealed a fairly healthy appearing person 68 in. tall, weighing 138 lb. The heart was not enlarged, no murmurs were heard, and the blood pressure was 130/80. Radiogram of the chest revealed no abnormality of the heart or lungs. The ballistocardiogram was normal.

The electrocardiogram obtained at rest showed occasional unifocal ventricular premature beats and nearly flat T waves in the extremity and left lateral chest leads. The electrocardiograms following exercise are shown in Figures 15 and 16. The changes following the Master two-step test were slight while those following a 5-min step test were regarded as having pathologic significance. It is seen that the diagnostic changes were confined to the ST segment. The low T waves changed minimally, but there was a perceptible anterior and superior rotation of the spatial T wave axis with widening of the QRS-T angle. A diagnosis was made of slight coronary heart disease with good functional reserve.

NORMAL MALE WITH ATYPICAL SYMPTOMS AND STRESS TESTS

CASE 10. A U. S. Navy officer, 42 years of age, was desirous of learning whether he was fit to engage in a very strenuous type of duty. His concern centered around the fact that for six or seven years he had noticed rather vague pains in the chest. The character of the pain varied but usually was in the nature of dull discomfort in the lower sternal region and epigastrium. The distress rarely was associated with exercise but frequently came on when he was under considerable mental stress. This distress might last for minutes, or for hours, and sometimes for "days on end." Rarely, he experienced a dull pain which never lasted longer than a few minutes and, on a few occasions, he was aware of slight numbness in the arms associated with this pain. At times he noted shortness of breath on slight effort, but usually he was able to exercise strenuously without undue dyspnea. For the previous two years, he had been aware occasionally of single premature beats which always distressed him even though he had been told that they had no pathologic significance. Physical examination revealed an unusually



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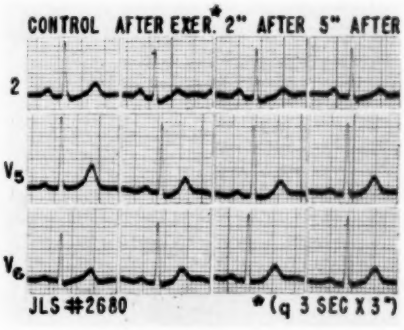

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Fig. 17 and 18. Case 10. Electrocardiograms after single and double Master tests and after strenuous single step test.

healthy appearing man, 70 in. tall, weighing 175 lb. The heart was not enlarged, the sounds were of good quality, and no murmurs were heard. The blood pressure was 140/90. The ballistocardiogram was normal. Radiogram of the chest revealed no abnormality of the heart and lungs. The blood serum cholesterol level was 174 mg per cent, and the atherogenic index 47.

The resting electrocardiogram was normal. Following a single Master test (Fig. 17), there was slight lowering of the RS-T junction in leads 2 and 3, and very slight lowering of the T waves in leads 2 and V_5. To evaluate better these very slight changes, a double Master test was carried out (Fig. 17), and the results showed a downward displacement of the RS-T junction of 0.5 mm in lead 2 together with other less significant changes. This depression of the RS-T junction was regarded as being due, in large part at least, to the effect of the auricular T wave. Moreover, this was in accord with the fact that the mean frontal plane vector of P was plus 70 degrees.

It was decided to do a more strenuous test which consisted of a 20-in. step-up every 2 sec for 3 min (Fig. 18). In lead 2, RS-T junction, which in the control record was approximately 0.5 mm below the baseline, was further displaced approximately 0.5 mm more. There was little or no RS-T junction depression in the other leads. Because of the fact that the significance of these changes was not clear, it was decided to carry out a 5-min step test at the rate of one step every 2 sec (Fig. 19). The patient noted only moderate dyspnea and felt that he could have continued the exercise for at least another minute or two. These observations were in line with the fact that the heart rate did not rise much above 100 beats/min. The RS-T junction was again displaced downward below the baseline approximately 0.5 mm in lead 2 and to a lesser extent in lead V_5. There was slight lowering of the T waves in these leads. Because the electrocardiographic alterations following the 5-min step test were not much different from those following lighter grades of work, the probability was small that these changes were due to acute myocardial ischemia.

NORMAL MALE WITH ABNORMAL ECG

Case 11. A U. S. Navy officer, 40 years of age, was referred for evaluation because of the electrocardiographic alterations disclosed in the course of an annual physical examination. He had always been unusually well and strong and had never been seriously ill. He had no symptoms referable to the cardiovascular system and considered himself in his usual state of good health. The heart was not enlarged, the sounds were of good quality, and a grade 1 systolic murmur was heard near the apex. The blood pressure was 116/74. Radiogram of the chest revealed no abnormality of the heart or lungs. The ballistocardiogram was normal. The blood serum cholesterol was 171 mg per cent, and the atherogenic index was 80.

The electrocardiogram, shown in Figure 20, revealed a prolonged PR interval and a QRS duration of 0.12 sec, with prominent S waves in lead 1 and an R′ in V_1.

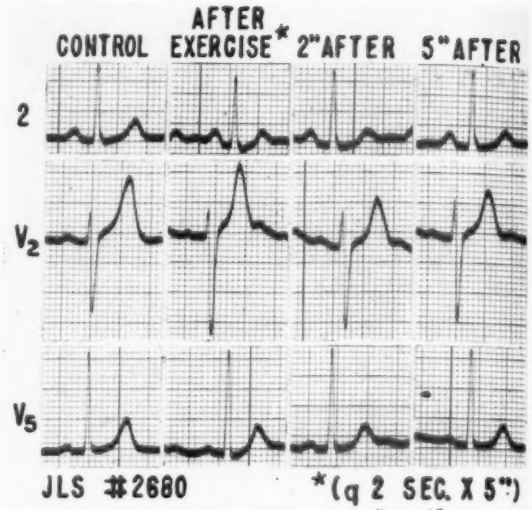
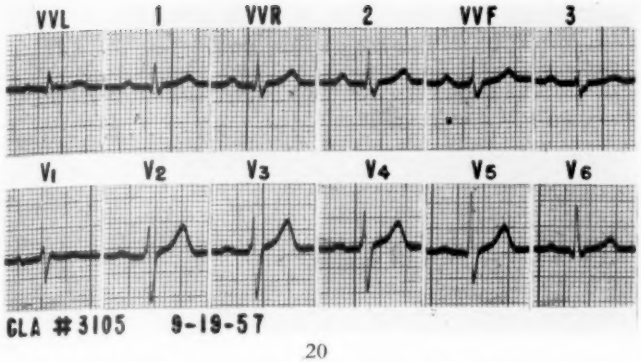


Fig. 19. Case 10. Electrocardiograms after more strenuous single step test.

The administration of 2 mg of atropine resulted in a change in duration of the PR interval from 0.22 sec to 0.18 sec. Levy's anoxia test was negative. There was no significant change in the electrocardiogram after 2 g of potassium chloride and after the administration of 100 per cent oxygen for 30 min. A double Master test produced no change in the electrocardiogram, not even a change in heart rate. Following strenuous exercise of one step-up every 3 sec for 5 min, there was slight shortening of the PR intervals but no other significant change, as can be seen in Figure 21. In view of the excellent response to strenuous exercise it was concluded that the conduction disturbances observed in the rest electrocardiogram were, in all likelihood, not due to coronary heart disease.

Case 12. A sergeant in the U. S. Air Force, 25 years of age, was referred for evaluation because of electrocardiographic abnormalities disclosed in the course of a routine re-enlistment examination. He has always been well and strong. More specifically, he had never had any symptoms suggesting pleurisy, pericarditis, or any disorder of the cardiovascular system. Physical examination revealed a healthy appearing person, 73 in. tall, weighing 205 lb. The heart was not enlarged, no murmurs were heard, and the blood pressure was normal. Radiogram of the chest revealed no abnormality of the heart or lungs. The ballistocardiogram was normal. The blood serum cholesterol was 204 mg per cent, and the atherogenic index 59.

The rest electrocardiogram showed frequent unifocal ectopic ventricular beats, and the T waves were nearly flat in all of the limb leads and in leads V_4 through V_6. There was no significant change in the electrocardiogram following the administration either of 2 g of potassium chloride by mouth or of 100 per cent oxygen for twenty minutes. After hyperventilation the electrocardiogram showed slight lowering of the T waves. The



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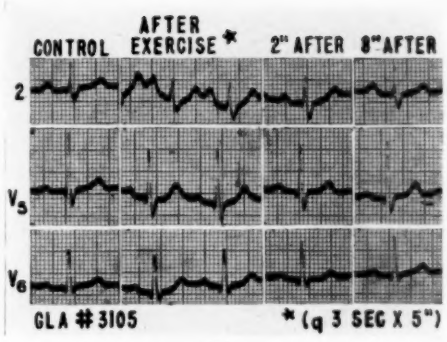

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Fig. 20. Case 11. Control tracing; equated limb leads. Fig. 21. Case 11. Electrocardiograms following single step test.

electrocardiogram after strenuous exercise, one step-up every 3 sec for 5 min, resulted in transitory elevation of all T waves but no significant RS-T segment changes.

Re-examination was carried out at our request ten months later. During the interval he had felt well and strong without any complaints. He was able to carry out strenuous exercise, one step-up every 2 sec for 5 min, with only a moderate degree of dyspnea. The improvement in configuration of the T waves was similar to that previously observed and is illustrated in Figure 22. We were unable to explain these electrocardiographic abnormalities but considered that they might represent a residuum of pericarditis. That they are due to coronary heart disease seems very unlikely.

PROLONGED PR INTERVAL AFTER EXERCISE

CASE 13. An applicant for flight training, 22 years of age, was referred for evaluation because of electrocardiographic alterations suggesting incomplete right bundle branch block. He had no complaints and had never been seriously ill. Physical examination revealed a healthy person, 72 in. tall, weighing 150 lb. The blood pressure was 126/76. The heart was not enlarged, no murmurs were heard, and the radiogram of the chest revealed no abnormality of the lungs or heart. The ballistocardiogram was normal.

The rest electrocardiogram revealed no abnormality, but the record obtained after strenuous exercise, one step-up every three seconds for five minutes, revealed temporary lengthening of the PR interval from 0.16 sec to approximately 0.23 sec. Diagnosis was deferred, and re-examination was carried out 5 months later. In the interim, the applicant was well and had no complaints whatever.

Following a single and a double Master test, there was no change in the PR interval. After a strenuous work test, one step-up every 2 sec for 3 min, there was a lengthening of the PR interval during recovery as shown in Figure 23. It is noteworthy that the lengthening of the PR interval did not occur immediately after exercise, the onset appearing in the record taken one minute after work and persisting for seven minutes. Although this is an unusual finding in a healthy person, it was believed

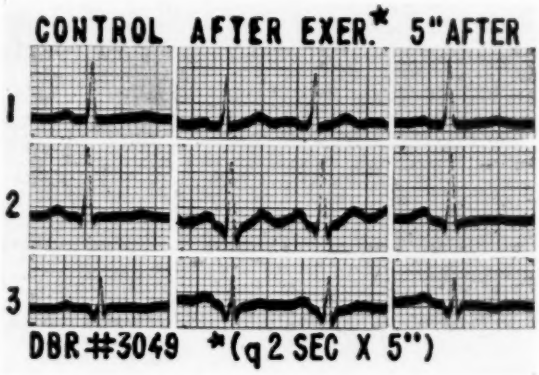


Fig. 22. Case 12. Electrocardiograms after strenuous one-step test.

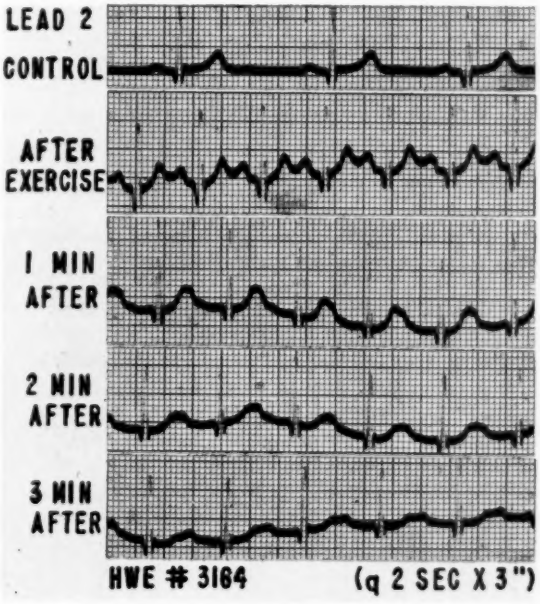
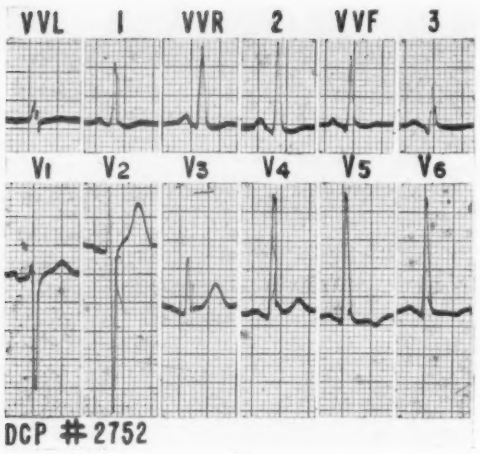


Fig. 23. Case 13. Electrocardiograms after strenuous work test. Note lengthening of PR interval with P superimposed on T in strip 3 and emergence of P in strip 5.



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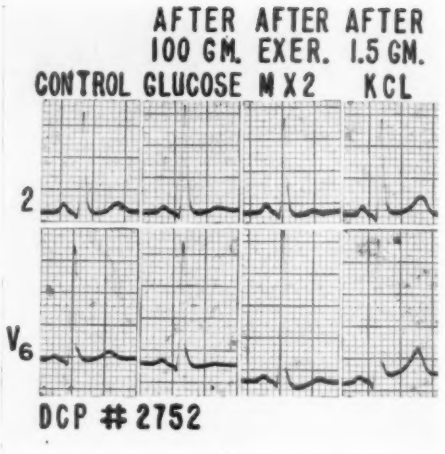

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Fig. 24. Case 14. Showing low diphasic or inverted T waves in electrocardiogram obtained from anxious young man.
Fig. 25. Case 14. Electrocardiograms after administration of glucose and potassium chloride and after double Master exercise test.

to represent an unusual heightening of vagal tonicity following exercise. The persistence of the phenomenon over a period of five months excluded the likelihood of an unusual degree of sensitivity due to acute toxicity. Coronary heart disease was considered not to be the causative agent.

The findings in this case might be compared with those in another apparently healthy young man, 20 years of age, whose electrocardiogram at rest showed prolongation of the PR interval and dropped beats. Following strenuous exercise, he had an electrocardiogram with the PR interval shortened to 0.26 sec for approximately 2 min, then lengthened again. Although disturbances in auriculoventricular conduction are often associated with underlying coronary heart disease, it is highly improbable that that was the etiologic agent in these two cases.

NORMAL MALE WITH LABILE T WAVES

Case 14. A 22-year-old airman was studied in an attempt to explain the low T waves in his electrocardiogram. He had no complaints whatever and had never been seriously ill. At the time of our examination he appeared apprehensive but in good health. He was 71 in. tall and weighed 175 lb. The heart was not enlarged, the blood pressure was 152/74. A grade 1 systolic murmur was heard in the pulmonic area and was thought to have no pathologic significance. Radiogram of the chest revealed no abnormality of the heart and lungs. Routine laboratory studies revealed no abnormalities.

The rest electrocardiogram (Fig. 24) showed considerable and unexplained variability in the amplitude of the T waves, particularly in leads 2, 3, V_5 and V_6 on different days. It was found that the T waves became normally upright following the administration of potassium chloride and that they became flat or diphasic after exercise or following the administration of glucose (Fig. 25). There was no significant change following the administration of 100 per cent oxygen. Because of the spontaneous variability and the circumstances under which the T waves could be altered, it was concluded that in all likelihood they had no pathologic significance.

Discussion

In our experience, exemplified in part by the cases presented, the use of various grades of exercise was helpful in the exploitation of the work electrocardiogram. Varying the work load was not only helpful in a qualitative sense, i.e., establishing the diagnosis of coronary heart disease, but also in a quantitative sense, i.e., estimating the degree of disability.

Diagnostic Value of Work Electrocardiograms: In the first group (cases 1 through 6) the diagnosis of coronary heart disease was based on findings other than those of the work electrocardiogram. Nevertheless, the electrocardiographic alterations following exercise provided evidence which greatly assisted in clarifying the degree of disability or in obtaining objective confirmation of the diagnosis. In the electrocardiogram of case 1, progressively greater T wave abnormalities were observed following three grades of light exercise. Without this information diagnosis would have been difficult, partly because of the vagueness with which the patient described his symptoms, and

partly because there were no other objective findings on which to base a definite diagnosis of coronary heart disease. This accounted for the fact that he had not been able to establish his claim for disability.

Case 6 illustrated the other extreme, in which a patient, having recovered from a minor but unequivocal coronary incident, demonstrated an excellent functional reserve. Without the results of the hard work tests, he would not have been returned to duty involving flying aircraft.

Case 4 exemplified the well-known fact that a patient with only moderate disability for coronary insufficiency might die suddenly of acute myocardial infarction.

The situation in case 3 was just the reverse, a patient with minimal coronary reserve who showed little change over a period of six years. Although there is a definite relation between the severity of coronary disease and the incidence of myocardial infarction, this relationship can be of significance only statistically and fails to take into account the many variables which can determine the occurrence of coronary thrombosis in a given individual.

The cases in the second group (cases 7 through 14) represented diagnostic problems in which the question of coronary heart disease had to be considered. Case 7 resembled case 1 in that the symptoms were vague and the patient was in the position of being a "prejudiced" observer. The objective evidence proved by the work electrocardiograms was helpful not only in making the diagnosis but also in establishing the degree of disability. Cases 8 and 9 illustrate the pertinent fact that significant electrocardiographic alterations may not appear after light exercise but frequently can be demonstrated after more strenuous work. We have noted this on numerous occasions and find that it is more frequent in athletic and physically fit individuals in their late thirties and early forties. Such men can perform the conventional exercise tests with such ease that their coronary reserve is not actually tested.

Case 10 illustrates still another type of problem where step-like increases in work load are helpful. In this instance, the electrocardiographic changes following light exercise might well have been interpreted as being pathologic. When the subject was exercised strenuously for five minutes, however, it became apparent that those changes were not significant because they were less pronounced, if anything. The failure to demonstrate progressively greater abnormality under progressively greater work loads was an important deciding factor.

In case 11 coronary heart disease was considered to be a good probability prior to the work tests. The fact that this patient was able to perform very strenuous exercise without distress and without any abnormality appearing in the electrocardiogram allowed us to conclude that the conduction disturbances seen in the rest electrocardiogram were unlikely to be due to coronary heart disease.

Type of Exercise Tests: With regard to our choice of type of exercise we are in agreement with Simonson and Keys[7] that walking on the treadmill is best. Walking is the most natural form of exercise, places less strain on tendon and joint than stair climbing, and the predetermined rate of work is held constant. The great disadvantage, of course, is that few physicians have access to the treadmill. With careful supervision, however, our single-step test provides not only a continuous work load, which is desirable, but also provides a great flexibility in terms of varying the rate, load, and duration of work. Exercise, equivalent in range from a slow walk to a fast run, can be scheduled. Master's two-step test does not provide a sufficiently high work load for persons with relatively good exercise tolerance nor does it permit the exercise to be "tailored" to the patient and his specific problem.

Choosing the proper rate of work poses an interesting problem. It is known that patients with angina of effort may experience pain on climbing a slight grade for some minutes, yet experience no distress after a short period of much more intense effort. Moreover, the patient with angina, after initially experiencing pain, may tolerate the same or even an increased work load without pain.[8] By analogy it would appear desirable to simulate the conditions under which angina is most likely to appear. On the other hand, if it is possible to produce

the diagnostic electrocardiographic alterations without distress to the patient, this seems highly desirable. Individual variation here may be important, but, in general, we have chosen a grade of exercise sufficient to produce considerable overload on the heart. This provides, in all probability, a favorable circumstance for detecting electrocardiographic changes due to acute coronary insufficiency and usually without provoking pain (cases 2, 3, and 7).

From a consideration of the medical findings and the exercise tolerance of the person to be tested, it is not difficult to decide on a safe amount for the initial test, as suggested by Manning.[9] Unless the initial exercise is light, more than one test should not be carried out on the same occasion; at least an hour should elapse between tests. Even assuming that Master's double two-step represents the single best rate and duration of exercise, we agree with Simonson and Keys[7] that much more intensive experience is needed before a definitive formulation can be made of the advantages of various grades of work in terms of rate, load, and duration.

Additional Electrocardiographic Tests: We have frequently made use of additional electrocardiographic procedures to assist in evaluating the results of the work electrocardiogram. Information has rarely been obtained from the *anoxia electrocardiogram* which was not obtainable from the work electrocardiogram, particularly in the evaluation of abnormal T waves. On the other hand, we have used with increasing frequency the *100 per cent O_2 test.* This consists of determining the effect of administering 100 per cent O_2 for 30 min. It is simple and safe but, unfortunately, is seldom positive. The abolition of RS-T and T wave abnormalities following oxygen administration and their return on withdrawal strongly suggests the presence of underlying coronary heart disease. Thus, for example, in case 13 the T waves were readily influenced by glucose, exercise, potassium chloride, and probably the sympathetic-parasympathetic stimulation associated with "anxiety," yet, they were not influenced by 100 per cent oxygen. In case 7 the administration of 100 per cent oxygen was followed by T wave changes in the direction of normal which greatly increased the probability that lowering of the T waves following exercise was due to myocardial ischemia.

Hyperventilation tests have been employed in many of our problem cases; we have observed lowering of the T waves but insignificant changes in the RS-T segment. Wasserburger *et al.*[10] have shown that even in healthy adult males hyperventilation may produce inversion of the T waves in two or more precordial leads in approximately 10 per cent of those tested. Since we frequently exercise our subjects strenuously, it is necessary to exclude the T wave changes of hyperventilation from those of exercise. In addition, in those patients whose abnormal T waves seem to be associated with anxiety, hyperventilation frequently intensifies the abnormality.

It is sometimes helpful to determine the amount of T wave change which can be produced by the *oral administration of glucose.* This is particularly true when a subject's serial tracings show unexplained variations. If these abnormalities can be reproduced by glucose, this possibility must be considered along with myocardial ischemia. It must be emphasized that lowering or inversion of the T waves following administration of glucose may occur in both the normal and abnormal heart.[11]

We have found it difficult to evaluate the changes following the *oral administration of potassium chloride.* Although, in general, our experience tends to confirm Grant's[12] belief that potassium will not restore abnormal T wave patterns caused by organic heart disease, exceptions have been noted. We have used a much smaller dose (1.5 g to 2.0 g) than most investigators[10–12] which explains the fact that frequently little change was observed.

In the majority of cases, *vectorial analysis of the T wave changes* has not been necessary in establishing a positive diagnosis. In a few instances, however, when exercise has caused both QRS and T axis displacement, constancy of the spatial QRS-T angle after exercise has been very helpful in delineating a normal from an abnormal response.[13]

Our limited findings do not justify conclusions regarding the relative significance of the various types or patterns of change in the work

electrocardiogram recently reviewed and evaluated by Lepeschkin and Surawicz.[14] However, they do suggest that no restrictions should be placed on the evaluation of all types of alterations in terms of the probability that they have significance. The present tendency to insist on a simple dichotomous separation between a "positive" and "negative" test result can only prevent the full exploitation of the work electrocardiogram. In our opinion, the work electrocardiogram should be analyzed and studied in much the same fashion as the rest electrocardiogram. This will yield many helpful clues and hints now buried in obscurity.

Summary and Conclusions

The value of the work electrocardiogram is discussed mainly on the basis of the findings in fourteen illustrative cases.

The importance of utilizing a wide range of work loads is emphasized. The determination of whether or not progressive electrocardiographic alterations occur with progressive change in work loads is always significant. In addition, it provides objective information not otherwise obtainable.

The use of the work electrocardiogram should not be limited to an attempt at a single dichotomous separation of patients suspected of having coronary heart disease into "positive" and "negative" categories. Rather, the attempt should be made to grade these patients along a continuum in terms of the probable degree of coronary sufficiency or insufficiency.

The full exploitation of the work electrocardiogram represents one of the most promising areas for development in clinical electrocardiography and should proceed along the conceptual lines established for the rest electrocardiogram. It is a long difficult undertaking beset with pitfalls, but the yield will make it worthwhile.

The 100 per cent oxygen test is deserving of wider usage.

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The Value of the Master Two-Step Test in Coronary Artery Disease*

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A STANDARDIZED exercise test is considered to be an important diagnostic aid in the detection of coronary artery disease. Although the two-step test as originated by Master[1] is the one usually employed, other authors[2–14] have varied both the method of performing such a test and the criteria of abnormality. This communication attempts to evaluate the criteria of abnormality and to enlarge upon the indications for the two-step test. The exercise test as developed by Master and other co-workers[15–21] is of accepted value in chronic coronary artery disease when the history is equivocal and the resting electrocardiogram is normal. It will be shown that the standardized exercise test is also of great value in two other situations: (1) when chest pain arises "de nuovo" and acute myocardial ischemia is suspected but cannot be so diagnosed (in which it has been thought by some to be dangerous) and (2) in the presence of an atypical history and an abnormal electrocardiogram.

MATERIAL AND METHODS

The material consists of Master two-step tests performed by 24 patients suspected of having coronary artery disease. In 12 patients the test was performed in the presence of a normal electrocardiogram to evaluate the significance of chest pain. In each case the diagnosis of coronary artery disease was in doubt. In six other patients the test was performed at a time shortly following (one week to two months) the development of "premonitory" pain. In 6 patients the test was performed in the presence of a non-diagnostic, abnormal electrocardiogram to assist in the diagnosis of angina pectoris. In all but one case the number of steps advocated by Master[1] for the double two-step test was employed. In one patient pain developed during the first minute and a half, and the test was terminated at that moment. For reasons discussed below, S-T depression of 1 mm or more in a classic lead or V_4 was considered an abnormal response.

RESULTS

The results of the Master two-step test performed by 24 patients are summarized in Table I. The patients are divided into four groups depending on the electrocardiographic response. *Group I* consists of fifteen patients in whom S-T depression in leads 1, 2, and V_4 are characteristic. In most of these patients the S-T depression in V_4 is greater than in classic leads 1 and 2. In only one patient is T wave inversion accompanied by S-T depression. *Group II* consists of three patients in whom T wave inversion occurs over the precordium. In two of these slight S-T depression over the precordium is also present. Only two patients are included in *group III*. In these two T became inverted in lead 1 and changed from inverted or isoelectric to upright in lead 3. *Group IV* consists of three patients in whom S-T depression and T wave inversion are present in leads 2, 3, and V_4. Finally, there is one patient who shows T wave inversion in V_2, V_3, and V_4.

In 10 patients pain occurred during the performance of the test; because of this, exer-

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TABLE I
Results of the Master Two-Step Test

Group	Patient number	Resting ECG	Premonitory pain	Pain with test	Depression of ST (mm)*			Inversion of T (mm)		
					Leads 1–2	Leads 2–3	V_4	Leads 1–2	Leads 2–3	V_4
I	1	LVH†	—	Yes	2	—	3	—	—	—
	2	Normal	—	—	1	—	3	—	—	—
	3	Normal	Yes	Yes	1 1/4	—	1 1/2	—	—	—
	4	LVH	—	—	1	—	0	—	—	—
	5	Borderline	—	—	0	—	3/4	—	—	—
	6	Normal	—	Yes	—	—	2	—	Yes	—
	7	Normal	—	—	1	—	1 1/2	—	—	—
	8	Normal	—	Yes	3/4	—	1 1/2	—	—	—
	9	LBBB‡	—	—	1	—	1	—	Yes	—
	10	Old infarction	—	Yes	1	—	1 1/2	—	—	—
	11	Borderline	—	Yes	3/4	—	1	—	—	—
	12	Borderline	—	—	1/2	—	3	—	—	—
	13	Borderline	—	Yes	1/2	—	—	Yes	—	+ −
	14	Normal	—	—	1 1/2	—	—	—	Yes	+ −
	15	Normal	—	—	1/2	—	1	—	—	—
II	16	Borderline	—	Yes	—	—	—	Yes	—	Yes
	17	Normal	Yes	—	—	—	1/2	—	—	Yes
	18	LVH	Yes	—	—	—	1	—	—	Yes
III	19	Normal	Yes	—	—	—	—	Yes	Up	—
	20	Normal	Yes	Yes	—	—	—	Yes	Up	—
IV	21	Borderline	Yes	Yes	—	3/4	—	—	Yes	+1
	22	LBBB	—	—	—	1	2	—	—	—
	23	Normal	—	Yes	—	—	1/2	—	Yes	Yes
V	24	Borderline	—	—	—	—	—	T inversion in $V_{2,3,4}$		

* Reference line—PQ segment.
† LVH—Left ventricular hypertrophy.
‡ LBBB–Left bundle branch block.

cise was stopped at this point. In general, electrocardiographic findings were maximal immediately after the completion of the test and usually lasted from three to five minutes. All electrocardiographic patterns had returned to the resting level at the end of seven minutes. In an occasional patient the most abnormal electrocardiogram might occur at the end of the second or fourth minute. Usually there was a real correlation between the severity of pain and the degree of S-T depression during the test. Ordinarily the electrocardiogram remained abnormal two or three minutes after the disappearance of pain, at which time the tracing rather rapidly returned to the resting level.

Discussion

The most frequently performed exercise test in general use appears to be the one developed by Master,[1] "using exercise over a one and a half or three minute period graded for weight and age." The criteria for abnormality, first stated in 1942,[16] are: "S-T depression greater than 0.5 mm in any lead or flattening or inversion of a T wave." With the advent of precordial lead electrocardiography, lead V_4 has been routinely taken in addition to the classic leads, apparently with no change in the previously established criteria.[21] Many authors have considered Master's criteria to be insufficiently strict. Twiss and Sokolow,[12] for example, believe that S-T depression should be

greater than 1 mm in lead 1, 1.5 mm in leads 2 and 3, and 2 mm in V_4. Mazer and Reisinger[6] set their limits on 0.75 mm in leads 1 and 3, 1.5 mm in lead 2 and 1.75 mm in lead IV. Most authors consider S-T depression in relation to the P-Q segment, but Grossman and Katz[4] have measured their segment depression from the isoelectric line.

Criteria for Abnormal Response: Only in recent years have sufficiently large groups of normals been studied using the Master two-step test. Wener *et al.*[20] have studied 311 "normals." Three per cent of these showed an abnormal "single" test and seven per cent showed an abnormal "double" test. Four of the 311 cases showed S-T depression greater than 1 mm. McGurl and Ross[22] in studying 247 normal men had abnormal responses in ten, or 4 per cent. Six of the ten cases had S-T depression greater than 1 mm. Leeds and Kroopf[23] studied 69 apparently normal women under age 35, six of whom showed a positive test according to Master's criteria. They concluded that the routine Master two-step test resulted in too many false positives and that an S-T depression of 1 mm should be an indication of abnormality. Thomas[24] studied 263 normal persons, using the double two-step test. She found S-T depression up to 1 mm in 41 patients and greater than 1 mm in only 6 persons. Finally, Simonson and Keys[25] discussed the normal controls of Master and concluded that deviations in S-T depression up to 1 mm represented random variations in a normal population and could not be considered abnormal.

Thus if 1 mm is a generally accepted dividing line between the normal and abnormal, more stringent criteria than those applied by Master would seem indicated. The results of this present study seem to confirm this belief since only one patient showed S-T depression less than 1 mm. All authors have emphasized the superiority of V_4 over the classical leads in demonstrating S-T depression. It is evident from the reported studies cited above that false positives do occur (3 to 5 per cent) and false negatives according to Master comprise up to 30 per cent of his series.

ECG Patterns in Positive Tests: Table I separates the patients into four distinct electrocardiographic patterns. In the majority of patients S-T depression over the precordium is the rule, presumably related to ischemia of the subendocardial layer of the left ventricle.[28] Similar changes in classic leads 2 and 3 are less common, and reciprocal S-T changes are unusual. Such findings parallel the distribution of electrocardiographic patterns in acute coronary insufficiency, as described by Cosby and his co-workers.[26]

T wave inversion is a relatively uncommon finding. When it occurs it is almost never accompanied by S-T depression. Thus, S-T depression and T wave inversion appear to be almost mutually exclusive.

In summarizing the results as shown in Table I, the electrocardiographic patterns during a positive exercise test consist primarily of S-T depression, usually in the precordial leads. The apparent area of cardiac involvement and the general contour of the S-T changes bear a close resemblance to the electrocardiographic patterns found in subendocardial infarction (acute coronary insufficiency).

Chest Pain and Double Two-Step Test: Divergent opinions have also been expressed as to the methods of performing the test in coronary artery disease. Scherf and Schaffer[10,11] have thought it unnecessary to standardize the test in terms of time, age or weight. Master and Storch[18] have maintained that a double two-step test should be performed only when the single two-step test is normal and then only after an hour's interval. All tests performed on patients in this present series were double two-step tests. In the ten patients who did develop pain, symptoms appeared between one and a half to three minutes in all but one case. The appearance of pain is an asset in the interpretation of the test. The hesitation of the patient, the occasional pallor and the description of the pain's slow onset and subsidence are quite dramatic and diagnostically significant. Just as important is the development of the abnormal electrocardiographic pattern immediately after the onset of such pain. There has been no patient in this series whose electrocardiogram failed to show abnormal features in the presence of pain. Thus, the performance of three minutes of exercise markedly influenced the

diagnostic value of the Master two-step test.

Indications for Two-Step Test: There are three indications for the use of a standardized exercise test. The usual indication is in the evaluation of an equivocal history of chronic or recurrent chest pain. There are two other situations in which the exercise test might be diagnostically useful; the first of these is in the presence of chest pain of recent duration in which the "premonitory" pain of coronary insufficiency or acute myocardial infarction is suspected, and a normal resting electrocardiogram is present. It may be thought by some authors[27,28] that in such a situation the small additional burden of exercise would be contraindicated. But when all other diagnostic methods are exhausted, the precipitation of pain, and thus the acquisition of an accurate and early electrocardiographic diagnosis, outweighs all other considerations. In six patients in this group an early positive two-step test accurately established a diagnosis not otherwise possible and resulted in the prompt initiation of therapy.

Another situation in which the exercise test is useful is in the presence of an abnormal electrocardiogram accompanied by a vague unsatisfactory history of chest pain. Six patients in the present series were examples of this situation. In these patients, dramatic S-T changes may be of great value in establishing the diagnosis of angina pectoris.

Conclusions

(1) The standardized exercise test performed according to the technic of Master is of inestimable value in confirming the diagnosis of angina pectoris and coronary artery disease. It should be employed in every patient with chronic angina pectoris, in whom the electrocardiogram is normal and gives important positive information in the majority of such patients. It may offer diagnostic information when myocardial ischemia is suspected, when normal electrocardiographic findings are present, and when other diagnostic means are exhausted. It is of definite value in the presence of an abnormal electrocardiogram when the diagnosis of angina pectoris is in doubt.

(2) The original Master criteria appear to be too liberal. S-T depression of 1 mm or more seems to be a more adequate separation of the normal response from the abnormal one.

(3) The importance of the double Master two-step test is emphasized. The highly diagnostic appearance of both pain and an abnormal ECG pattern occurs more often during the second minute and a half of this test.

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Duration of the Normal P Wave*

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THE PRECISE duration of the P wave is important in correlative studies in clinical electrocardiography, in the use of the electrocardiogram to time physiologic events such as heart sounds and vascular pressure curves, and in the measurement of the P-R interval. Although the P wave is usually the simplest of all electrocardiographic waves, the range of normal values for its duration, as proposed by different authors, varies considerably, as shown in Table I. The variability of the accepted range limits the clinical usefulness of the measurement of the P wave duration. The reported variability reflects the difficulty encountered in measurement due to the small size of the wave and the use of different leads in measuring the duration.

The present study was performed to determine if it were possible to obtain better definition of the duration of the P wave to enhance its clinical significance.

METHODS AND MATERIALS

The P wave durations were measured on 50 electrocardiograms recorded on heat-sensitive paper by direct-writing electrocardiographs, with a paper speed of 25 mm per second. All tracings were obtained from males previously found healthy by thorough medical evaluation. The subjects had an average age of 34 years. Twenty were between 20 and 30 years, 17 between 30 and 40, 11 between 40 and 50, one was 52, and another, 82 years of age.

The P wave was measured in each of the three standard leads, the three augmented unipolar leads, and the six routinely taken precordial unipolar leads. The onset of the wave was defined as the point of the first visible upward departure of the trace from the bottom of the baseline for the positive waves, and as the point of first visible downward departure from the top of the baseline for negative waves. The return of the bottom of the trace to the baseline in positive waves, and of the top of the trace in negative waves was considered to be the end of the P wave (Figs. 1 and 2). Measurements were performed with calipers from images of the tracings magnified ten times utilizing an electrocardiographic enlarger.

TABLE I

Accepted Ranges of Normal for P Wave Duration in Adults

Source	Comment
Rushmer[1]	"around 0.08 sec"
Barker[2]	"not over 0.10 sec"
Burch and Winsor[3]	"does not normally exceed 0.11 sec"
American Heart Association[4]	0.06 to 0.11 sec
Sodi-Pallares[5]	0.12 in lead 1 abnormal
White[6]	"not over 0.1 sec" in lead 2
Grant[7]	0.12 sec or more considered a prolongation
Lepeschkin[8]	0.07 to 0.12 sec
Katz[9]	"between 0.10 and 0.12 sec viewed with suspicion . . . over 0.12 abnormal"
Graybiel[10]	0 to 0.12 sec

RESULTS

The distribution of the values of the durations of the 600 P waves from the 12 leads of the 50 electrocardiograms are shown in Figure 3. The range of the P wave duration was 0.000 to 0.178 sec. The zero value refers to five instances when a P wave was not seen in a given lead. Table II presents the range and average

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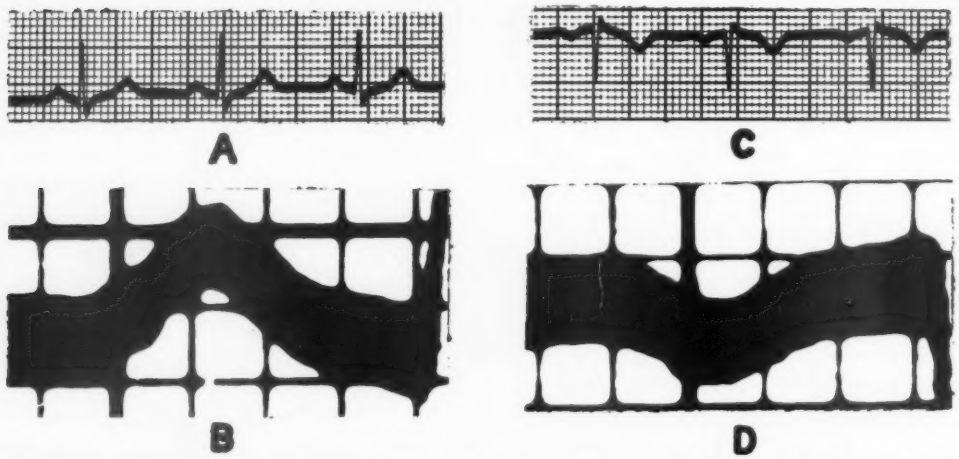

Fig. 1. Comparison of actual-size electrocardiograms and P waves enlarged 10 times. (A) Lead 2. The P wave in the center complex, in routine practice, measured 0.10 second. (B) The P wave of (A) enlarged 10 times. The first visible upward departure of the trace from the bottom of the baseline occurs 0.01 sec before the thicker 0.20 time line. The return of the bottom of the trace to the baseline occurs 0.13 sec after the beginning of the wave. (C) Lead aVR. In routine practice the P wave, obscured by the time lines, measured 0.08 sec. (D) The P wave of (C) enlarged 10 times. Time lines are more clearly seen and the P wave measures 0.10 sec.

values for the duration of the P wave in each lead. The average duration of the 600 P waves was 0.101 sec. The average of the minimum P wave durations was 0.071 sec with the shortest P wave duration occurring in aVL. The average of the maximum durations was 0.130 sec. Of the 50 subjects 44 had a P wave duration of 0.12 sec or greater in one or more leads. Leads aVF and V_5 most often showed the maximum P wave duration (Table III). Leads aVR, aVF, and V_4 were the leads that most often had a P wave duration of 0.12 sec or longer (Table IV).

The maximum P wave duration was found in one of the precordial leads in 24 subjects. In 21 of these 24 subjects the maximum duration was 0.12 sec or greater. In 15 of the latter 21 subjects a P wave of 0.12 sec or longer appeared in one or more of the limb leads.

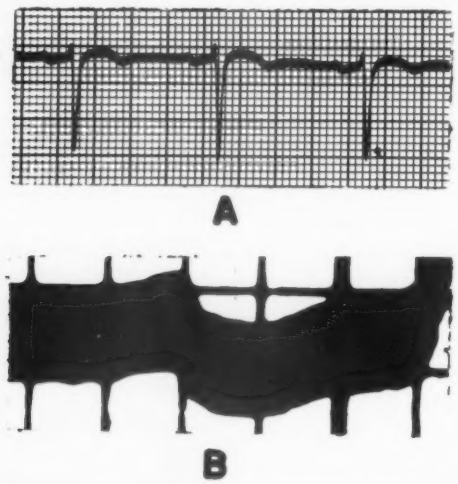

Fig. 2. (A) Lead V_1 from the same subject in Figure 1. (B) Diphasic P wave from the center complex of (A) enlarged 10 times. Measurement of P duration from upward departure of the bottom of the baseline in the positive portion of the wave to the return of the top of the trace to the baseline in the negative portion of the wave is 0.12 sec.

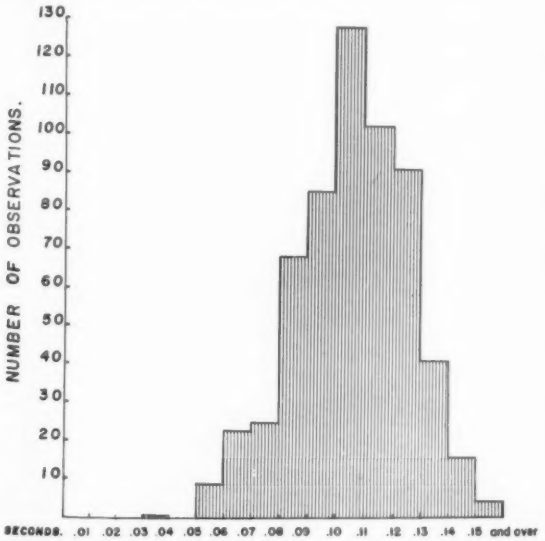

Fig. 3. P wave durations in 50 normal electrocardiograms (600 measurements).

TABLE II

Duration of the P Wave in 50 Electrocardiograms

	Time in seconds		
Leads	Maximum	Average	Minimum
1	0.160	0.096	0.054
2	0.130	0.108	0.060
3	0.142	0.098	0.048
aVR	0.135	0.110	0.074
aVL	0.130	0.088	0.038
aVF	0.178	0.109	0.056
V_1	0.134	0.091	0.050
V_2	0.146	0.094	0.044
V_3	0.160	0.100	0.048
V_4	0.150	0.109	0.070
V_5	0.140	0.108	0.070
V_6	0.135	0.105	0.062

TABLE III

Frequency of Occurrence of Maximum P Wave Duration

Lead	Subjects
1	4
2	2
3	5
aVR	6
aVL	4
aVF	12
V_1	2
V_2	2
V_3	4
V_4	8
V_5	10
V_6	6

Age did not affect the values. Since the rate in the electrocardiograms studied was within normal limits it was not a consideration in P wave duration.

Discussion and Conclusions

Values of P wave duration obtained from averages of P waves in all leads or in specific leads did not represent the maximal P wave duration found in a normal subject's electrocardiogram. The maximal duration encountered in the 12-lead electrocardiogram was considered the measurement most accurately representing atrial electrical activity, although it is conceivable that the entire P wave may not be represented in any of the conventionally recorded 12 leads. The lead in which the maximal duration is encountered could not be predicted (Tables III and IV). Leads in which the P wave measures less than the maximal duration should not be considered representative of atrial electrical activity and should not be used for electrocardiographic measurement or to time physiologic events.

TABLE IV

Frequency of Occurrence of P Wave Duration of 0.12 Second or Greater

Lead	Subjects
1	6
2	15
3	14
aVR	21
aVL	6
aVF	21
V_1	5
V_2	5
V_3	12
V_4	18
V_5	13
V_6	14

Forty-four of 50 normal subjects had P wave durations of 0.12 sec or greater in one or more leads. The average maximum P wave duration was 0.13 sec. These measurements reflect the precision gained by magnification of the tracings with consequent better definition of the waves and improved determination of the points of departure and return of the trace from and to the baseline. These findings suggest that the P wave duration generally exceeds that accepted as normal[1–11] and that P waves of less than 0.12 sec may not be representative of atrial electrical activity.

Summary

Accurate use of the P wave in electrocardiographic measurement and in electrocardiographic timing of physiologic events requires prior study in each individual to determine the lead with the maximal P wave duration. Magnification of electrocardiographic waves is useful to determine their duration.

The duration of the P wave in the electrocardiograms of 50 normal males was found to exceed the accepted normal. Criteria for normal P wave duration based on average values of the duration in all leads or average values of

the duration in specific leads are not representative of maximal P wave duration in the electrocardiogram.

Maximal P wave duration must be considered most representative of atrial electrical activity. P waves of less than 0.12 sec in duration should not generally be considered representative of atrial electrical activity in normal subjects.

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Auricular Overloadings

Electrocardiographic Analysis of 193 Cases*

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CONSIDERABLE attention has been paid in recent years to the electrocardiographic patterns produced by hypertrophy and dilatation of the ventricular chambers;[1–5] however, only a few studies have concerned themselves with the problem of the auricular overloadings.[6,7]

Besides the fact that the atria share, to a greater or lesser extent, consequences of almost all conditions giving rise to ventricular overloadings, certain other situations, namely stenotic outlets of the atria, manifest their effects predominantly on the auricles themselves. Careful interpretation of the auriculogram, both morphologic and vectorial, can impart considerable information regarding such overloadings.

In addition to these pathologic entities, the auriculogram is also subjected to alteration under a variety of physiologic conditions which are important to be considered. These are: (1) respiration, (2) neurovegetative stimuli, (3) physical exertion, (4) and above all the variations in the anatomic position of the heart. It is well known that during deep inspiration, as a result of downward displacement of the diaphragm, the P vector tends to deviate downward and rightward; in deep expiration the opposite occurs. Physical exertion tends to increase the voltage of the P wave in the limb leads, probably as a result of two factors: (1) mechanical—increase in the work of the auricles because of augmented cardiac output; (2) neurovegetative—sympathetic overactivity. The neurovegetative influences are exerted through the autonomic innervation of the atria, the P wave increasing in voltage with sympathetic stimulation and decreasing with parasympathetic overactivity.[8]

Finally, the anatomic position of the heart plays an important role in the localization of the mean auricular vector (SAP). In the so-called vertical heart, this vector in the frontal plane generally lies between +50 and +75 degrees, while in the horizontal heart the auricular axis ranges from +30 to +45 degrees. Similarly pregnancy, through diaphragmatic elevation, causes leftward deviation of the P vector. Chest deformities, as for instance pectus excavatum, frequently cause changes in both the morphology of the auricular wave and the localization of the P vector.[9,10] In cases of dextrocardia, the alteration in the position of the mean atrial vector is very characteristic.[6]

Many criteria have been established regarding the normal patterns of the P wave and the normal range of the P vector. A normal P wave in the limb leads should not exceed 0.10 sec in duration and 2.5 mm in amplitude. It is also accepted that a normal auricular wave should not show notching or peaking in its morphology.[11] The P vector in the frontal plane is supposed to confine itself between +30 and +75 degrees. A wider range to the left has been described in normal individuals, however never exceeding −30 degrees.[12] Similarly, in the horizontal plane, a normal atrial vector characterizes itself by pointing either forward or being parallel to the frontal plane. In a few instances we may find the auricular vector oriented slightly backward. Assuming that the transitional plane of the auricular electric field passes through the vicinity of the exploratory electrode of V_1, the pattern of the P wave in this lead is a guide to the determination of the atrial vector in the horizontal plane. Thus,

* From the Marie L. Coakley Cardiovascular Laboratory, St. Vincent Charity Hospital, Cleveland, Ohio.

whenever the area of positivity predominates over the negative phase of the P wave, the vector is pointing forward, while it is directed backward in the contrary situation. In the event of both positive and negative phases being equal, the vector is placed parallel to the frontal plane.

Zuckermann[13] describes three types of pathologic P waves: (1) P "mitrale"—characterizing typical left auricular overloading; (2) P "congenitale"—found in patients with congenital heart lesions, manifesting right atrial overloading; (3) P "pulmonale"—that appears in cases of chronic pulmonary diseases particularly with emphysema, in the presence or absence of "cor pulmonale." It seems important to point out that in many cases of chronic pulmonary disease, there does not exist any evidence of right atrial overloading, the changes observed in the P wave and in the P vector being caused by other factors which will be stressed later.

Material and Methods

In order to evaluate the efficiency of the established criteria for the diagnosis of the auricular overloadings, we have performed an electrocardiographic analysis of the P wave and the P vector in 193 patients hospitalized in St. Vincent Charity Hospital during the past three years, with the diagnosis of mitral valve lesions, congenital cardiac malformations, and chronic pulmonary diseases In many cases, hemodynamic and vectorcardiographic correlations were made.

The diagnosis of chronic pulmonary disease was accepted on clinical and radiologic grounds, but all cases of mitral valve lesions and congenital cardiac malformations selected for this study also had hemodynamic evaluation. Additional confirmation by operative notes or necropsy studies were added whenever available.

The electrocardiographic analysis in each patient included the study of: (1) longest duration and largest amplitude of the P wave in the limb leads; (2) presence of notching or peaking in the auriculogram; (3) the morphology of the atrial wave in V_1-V_2 and V_5-V_6; (4) the spatial localization of the mean auricular vector (SAP), by using Grant's method for its determination in the frontal plane[14] and considering lead V_1 as being in line with the perpendicular thoracic projection of the auricular electrical center in order to establish the vectorial orientation in the horizontal plane; (5) the index of Macruz.[15]*

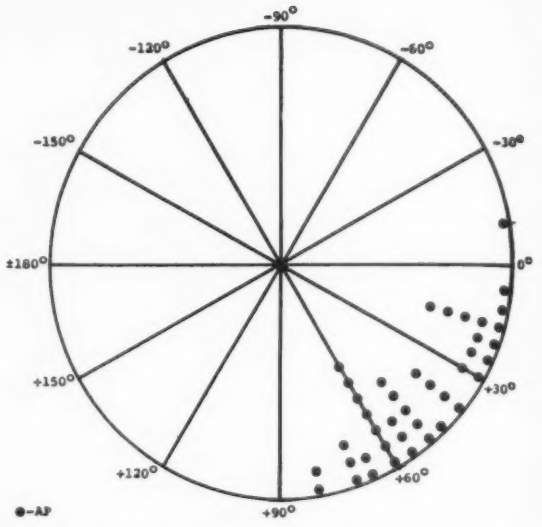


Fig. 1. The distribution of the P vector in the frontal plane in 41 patients with mitral lesions.

The vectorcardiographic study was performed by applying the method of the tetrahedron of Wilson. The P loops were isolated by means of an electrical dissection system.† The pictures were taken by a polaroid Land camera. The direction of inscription of the auricular loops was determined in the three planes and a particular study was carried out in the sagittal plane.

All cases in which any influence of the physiologic conditions previously referred to possibly existed were excluded from this study. Patients with atrial fibrillation or flutter were not included for obvious reasons.

Results

Mitral Valve Lesions

All 41 patients in this series had dilated and/or hypertrophied left atria demonstrated by surgery or autopsy. Their ages varied from 16 to 47 years. Electrocardiographic analysis was as follows:

SAP: Figure 1 shows the distribution of the

* This index is the ratio between the duration of the P wave and the P-R segment in the limb leads. Normal values range between 1.0 and 1.6, a value lower than this being taken as evidence for right atrial and a higher one for left atrial overloading.

† This dissection system was built in our Research Department by Mr. Harrison A. Zieske, Jr.

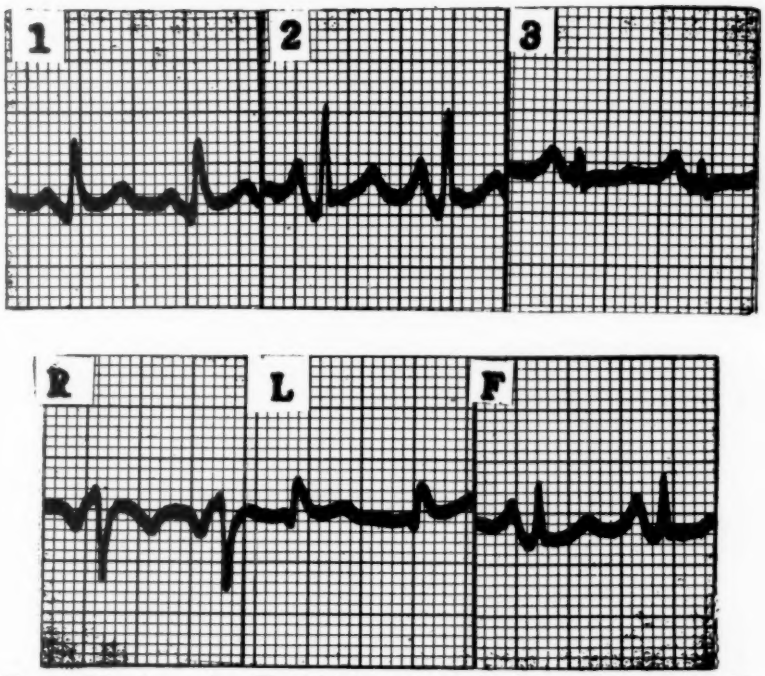


Fig. 2. Mitral stenosis. The AP is beyond +60°. Pressures were elevated in both right atrial and ventricular chambers. See text.

mean auricular vector in the frontal plane. It varied from −10 degrees to +85 degrees. This distribution of the atrial axis could be divided as follows:

(1) Tendency to deviate to the left (from −10 to +30 degrees)	14 cases
(2) No tendency to deviate (from +35 to +60 degrees)	20 cases
(3) Tendency to deviate to the right (from +65 to +85 degrees)	7 cases

In all seven patients in whom the P axis was beyond +60 degrees, there were increased pressures in both right auricular and ventricular chambers. Two of the patients also had, as it was shown during surgery, an associated tricuspid stenosis (Fig. 2). In the horizontal plane the auricular vector was pointing forward in 4 cases (10 per cent), backward in 33 patients (80 per cent), and parallel to the frontal plane in the remaining 4 (10 per cent).

Duration in the Limb Leads: The largest duration of P varied from 0.09 to 0.14 sec, the average being 0.12 sec.

Amplitude of P in the Limb Leads: The greatest amplitude of P ranged from 1 mm to 3.6 mm. It exceeded 2.5 mm in three cases and 3.0 mm in two. It seems interesting to point out that 4 out of these 5 patients were in the group of 7 in whom the AP was directed rightward beyond +65 degrees. It is also important to stress that in the case in which there was no right auricular overloading, the increased amplitude (3.2 mm) appeared in the second part of the atrial wave, which probably indicated hypertrophy of the left atrium (Fig. 3).

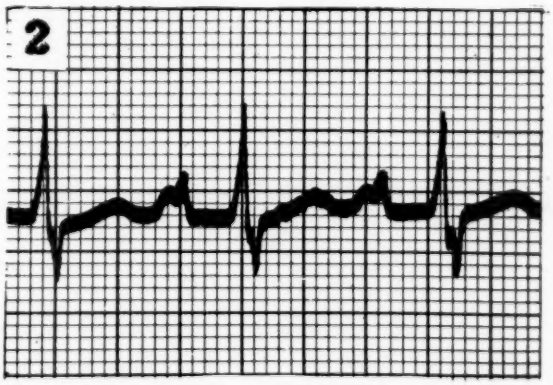


Fig. 3. Mitral stenosis. The increased amplitude appears in the second part of the P wave, indicating left atrial hypertrophy.

Morphology of P in the Limb Leads: The P wave showed notching in 24 cases, most commonly in leads 1 and 2 and in a few cases in 3 and aVF.

Precordial Leads: Lead V_1: The P wave showed a ± morphology in 32 cases; there was a predominance of the positive phase in one case, the negative area was larger in 27 cases and both phases were equal in 4 patients. In six cases the P wave was completely negative (−), and in three it was completely positive (+).

Leads V_5 and V_6: In 30 patients the duration of the P wave exceeded 0.10 sec. In 15 cases the auricular wave showed notching in these leads.

Index of Macruz: It was below 1.0 in two cases; between 1.0 and 1.6 in 15 cases and above 1.6 in 24 cases. As one can see, the index of Macruz was positive for left auricular overloading, according to the above author's criteria,[15] in only 24 patients or 59 per cent of the total. Of the 17 cases in which this index was within normal limits or pointing to right auricular overloading, in six there was first degree block (P-R interval longer than 0.21 sec) and in four there existed increased right atrial pressures.

PULMONIC STENOSIS

The electrocardiograms of 20 cases of pure pulmonic stenosis were studied. The ages of the patients varied from 5 months to 28 years. The findings were as follows:

SAP: It varied from +20 degrees to +70 degrees in the frontal plane; the average being +49 degrees. In the horizontal plane it was oriented forward in 16 cases, parallel to the frontal plane in 3 cases, and backward in one.

Duration of P in the Limb Leads: It varied from 0.05 sec to 0.08 sec.

Amplitude of P in the Limb Leads: It ranged from 1.0 mm to 3.3 mm, the average being 1.9 mm.

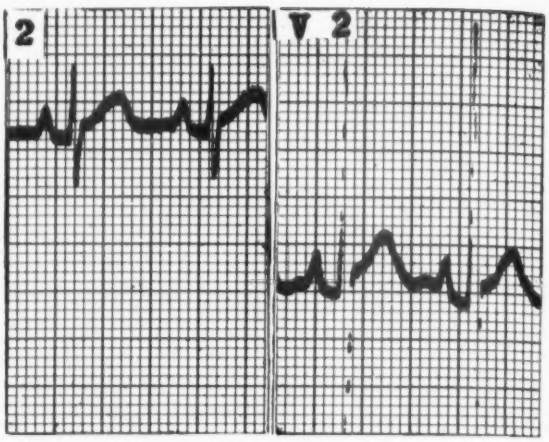


Fig. 4. Peaked and tall P waves (above 2 mm) in leads 2 and V_2 in a patient with pulmonic stenosis and systolic pressure in the right atrium above 10 mm Hg.

Morphology of P in the Limb Leads: It showed a peaking morphology in 14 cases in one or more limb leads.

Precordial Leads: Lead V_1: The P was predominantly positive in 16 cases, negative in one and displayed equal areas of positivity and negativity in the other 3 cases. The largest amplitude in this lead was 1.5 mm. In 12 patients this wave showed a peaking morphology.

Lead V_2: The P was peaked in 13 cases. In 6 cases the peaking morphology extended up to V_4 and in 2 patients up to V_6. The largest amplitude in the lead was 3.5 mm.

Index of Macruz: It was below 1.0 in 13 cases, between 1.0 and 1.6 in 5 cases, and above 1.6 in 2 cases.

Correlation with Hemodynamic Findings: Attempting to correlate the appearance of peaking and the amplitude of the P waves in both the limb and the precordial leads, with the pressures in the right auricle and the right ventricle and

TABLE I

Relationship Between the Amplitude and Morphology of the P Waves and the Systolic Right Atrial Pressure in 7 Patients with Pulmonic Stenosis

Cases	1	2	3	4	5	6	7
Systolic right atrial pressures in mm Hg	15	12	15	10	13	10	11
Largest amplitude of the P waves in the limb leads in mm	1.9	3.3	3.0	2.2	1.5	1	1.8
Amplitude of the P waves in V_2 in mm	3.5	1.6	2.2	2.5	2.2	2.1	2.5
Morphology of P waves in the limb leads and V_2	Peaked	Peaked	Peaked	Peaked	Peaked	Peaked	Peaked

TABLE II

Correlation of the Right Atrial Pressures and the Arterial Saturation with the Amplitude and Morphology of the P Waves in 16 Cases of Tetralogy of Fallot

Cases	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Pressures in R.A. in mm Hg	5.5/2.5	11/1	16/5	13/3	5/1.5	6/2	7/3	5/0	9/5	17/10	2.5/2.5	12/1.5	8/2	14/9	4/1	18/12
% Arterial saturation	85.6	82.0	73.0	74.0	91.6	93.4	82.0	81.2	92.0	69.9	88.2	88.0	71.1	87.0	90.0	67.0
Largest amplitude of the P waves in the limb leads in mm	1.4	2.6	3.6	4.0	1.8	1.8	2.0	2.2	1.8	4.0	1.5	2.5	2.2	2.6	1.0	3.8
Amplitude of the P waves in lead V_2 in mm	1.6	2.8	1	2.5	0.8	1	3.1	1.8	0.8	1.2	0.5	1.8	1	0.5	1.0	1.8
Morphology of the P waves in the limb leads	N	P	P	P	N	sP	P	sP	sP	P	N	P	P	P	N	P
Morphology of the P waves in lead V_2	sP	P	P	P	N	sP	P	P	sP	P	sP	P	sP	sP	sP	P

N = Normal. P = Peaked. sP = Slightly peaked.

also with the arterial oxygen saturation, we found:

(1) Whenever the systolic pressures in the right auricle were increased (10 mm Hg or more), the amplitude of the P wave was always larger than 2 mm, either in one limb lead or in V_2 and in some records in both (Fig. 4).

In all of these patients, the P wave showed a more or less peaking morphology (Table I).

(2) In the absence of increased right atrial pressures, even in the presence of very high right ventricular pressures, the amplitude of the P did not reach 2.0 mm, although this wave showed a peaking morphology.

(3) In one case in which the right atrial pressures were normal (3/0) and the right ventricular were only slightly elevated (50/0), we found very tall peaked P waves in the limb leads (2.6 mm) and in V_2 (3.5 mm). It seems important to point out that this patient was the only one in this series showing arterial oxygen desaturation (84 per cent).

TETRALOGY OF FALLOT

Sixteen cases were analyzed in this group. The ages varied from 10 months to 43 years. The results were as follows:

SAP: It ranged from +20 degrees to +85 degrees in the frontal plane. In one patient it was located at +105 degrees but an associated dextrocardia was responsible for this. In the horizontal plane the mean auricular vector was oriented forward in 11 cases, backward in 4 cases, and parallel to the frontal plane in one.

Duration of P in the Limb Leads: It varied from 0.05 sec to 0.09 sec.

Amplitude of P in the Limb Leads: It ranged from 1 mm to 4 mm, the average being 2.4 mm.

Morphology of P in the Limb Leads: The P wave was markedly peaked in 9 cases, slightly peaked in 3 cases, and normal in 4 cases.

Precordial Leads: Lead V_1: In 11 cases the P wave was totally or predominantly positive. It showed a predominance of negativity in 4 cases and the areas of positivity and negativity were both equal in one. In 5 patients the P wave showed a marked peaking morphology.

Lead V_2: The P wave was peaked in 14 cases. The largest amplitude in this lead was 3.8 mm. In 7 patients the peaking morphology was extended to the left precordial leads.

Index of Macruz: It was below 1.0 in 13 cases, between 1.0 and 1.6 in 2 cases, and above 1.6 in one case.

Correlation with Hemodynamic Data: Attempting to correlate the amplitude and the morphology of the P waves in both limb and precordial leads with the hemodynamic data, we have found:

(1) Similar to the cases of pure pulmonic stenosis, whenever the systolic pressure in the right atrium was equal to or more than 10 mm Hg, the voltage of the P wave was larger than 2 mm in one of the limb leads (generally lead 2), and a peaking morphology was present (Table II).

(2) In those cases in which the systolic pressure in the right atrium was normal but the

arterial saturation was below 85 per cent, peaked P waves exceeding 2 mm in amplitude were present either in the limb or precordial leads (Table II).

(3) When the right atrial systolic pressure was normal and the arterial saturation was above 85 per cent, the P waves, although showing in some cases slight peaking morphology, never exceeded 1.8 mm in amplitude (Table II).

(4) The patients presenting the combination of higher right atrial systolic pressures and arterial desaturation below 80 per cent were those who had the largest amplitudes of P waves in the limb leads (Fig. 5 and Table II).

INTERATRIAL SEPTAL DEFECT

In this series we have analyzed the electrocardiograms of 50 cases of atrial septal defects of the "ostium secundum type." In 6 of them there was associated partial anomalous drainage of the pulmonary veins into the right auricle. Patients presenting persistence of the common atrioventricular canal were not considered here, being analyzed elsewhere in this paper. The ages of the patients ranged from $3^1/_2$ months to 48 years. The average age was 14 years. The analysis was as follows:

SAP: The auricular vector varied from +10 to +85 degrees in the frontal plane. In the great majority of these cases (40 patients), the P axis ranged from +30 to +60 degrees. In seven cases there was a tendency of the auricular vector to deviate to the right (from +65 to +85 degrees). In three patients the AP showed slight deviation to the left (from +25 to +10 degrees). In the horizontal plane, the mean auricular vector was oriented forward in 28 cases, backward in 10 cases and parallel to the frontal plane in 12.

Duration of P in the Limb Leads: The duration of the P wave in 45 cases was equal to or less than 0.10 sec, and in 5 cases it was more than 0.10 sec, although not exceeding 0.12 sec.

Amplitude of P in the Limb Leads: It varied from 0.8 to 2.6 mm, the average being 1.5 mm. In only four cases the P wave was taller than 2 mm.

Morphology of P in the Limb Leads: It was normal in 32 cases, slightly peaked in 14 cases and notched in 4. Those patients in whom there existed notchings in the P wave also presented increase in the duration of this wave. This could be explained as meaning slight degree of left auricular overloading, as a consequence of augmented pulmonary venous return.

Precordial Leads: Leads V_1 and V_2: We found peaked P waves exceeding 1.5 mm in amplitude in V_1 and/or V_2 in 31 cases. In a previous paper[16] we have correlated the P wave pattern in

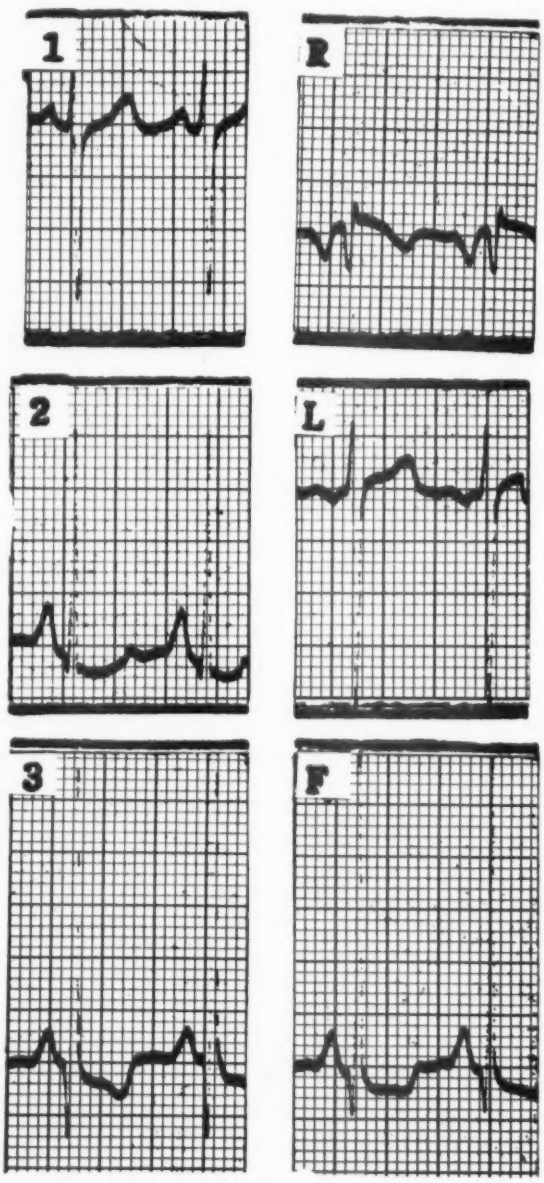


Fig. 5. Tetralogy of Fallot. Extremely tall P waves in a patient presenting both high atrial systolic pressure and arterial oxygen desaturation below 80 per cent.

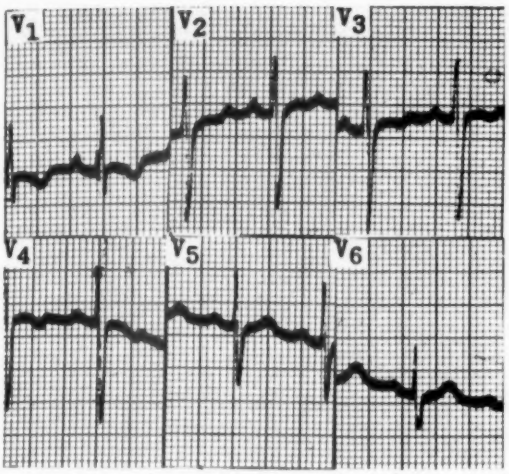


Fig. 6. Interatrial septal defect. Peaked P waves in V_1-V_2 in a patient with a shunt flow of 93 per cent.

right precordial leads with the hemodynamic data, and we demonstrated that the morphology of the P wave in V_1 and V_2 bears some relationship with the magnitude of the left-to-right shunt through the defect (Fig. 6).

No definite correlation could be found between either the amplitude or the morphology of the P wave and the pressures in the right auricular chamber.

In all cases the auricular waves could be considered normal in the left precordial leads.

Index of Macruz: It was below 1.0 in 27 cases, between 1.0 and 1.6 in 15 cases, and above 1.6 in 8.

TRANSPOSITION OF THE GREAT VESSELS

We have studied the electrocardiograms of five children who had complete transposition of the great vessels demonstrated by autopsy. The ages of these patients varied from 12 days to 10 years.

SAP: It ranged from +30 to +65 degrees in the frontal plane. In the horizontal plane it was oriented forward in four cases and backward in one.

Duration in the Limb Leads: It was less than 0.10 sec in three cases and more than 0.10 sec in the other two (0.11 sec).

Amplitude in the Limb Leads: It varied from 1.8 mm to 4.5 mm, the average being 3.5 mm.

Morphology in the Limb Leads: The P waves were peaked in all cases.

Precordial Leads: Lead V_1: The P wave was entirely positive in three cases. A plus-minus pattern was present in the other two; in one of them the positive phase was predominant and in the other one the negative area was larger. The largest amplitude in this lead was 2.6 mm. In all cases the auricular wave was peaked.

Lead V_2: In all cases the P waves were peaked and positive.

Leads V_5 and V_6: The P waves were peaked in three cases. In the other two they were notched and increased in duration (0.10 and 0.11 sec). It seems interesting to point out that these two patients were those who also showed enlarged P waves in the limb leads.

Index of Macruz: It was below 1.0 in one case, between 1.0 and 1.6 in two cases and above 1.6 in the other two.

Correlation with Hemodynamic Data: The inter-

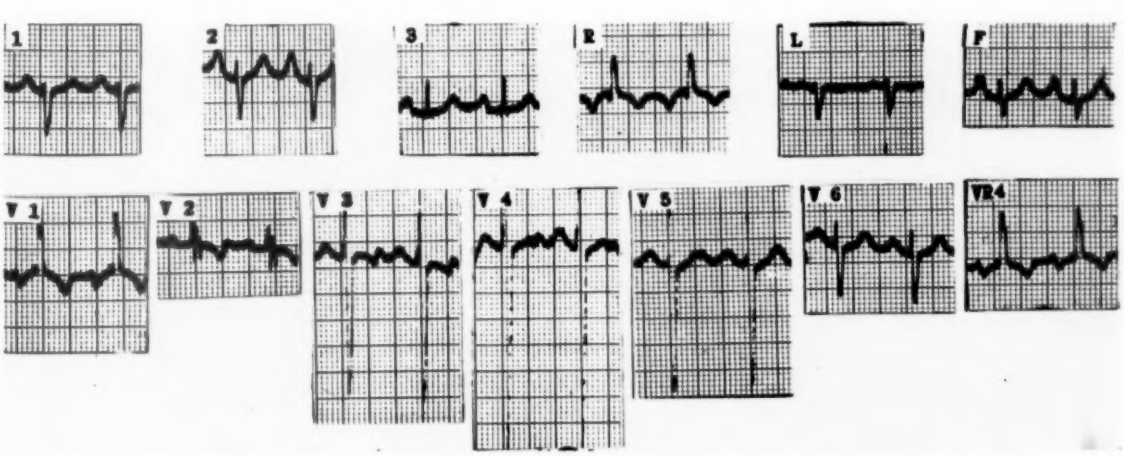


Fig. 7. Transposition of the great vessels. Tall and wide P waves suggesting biauricular overloading.

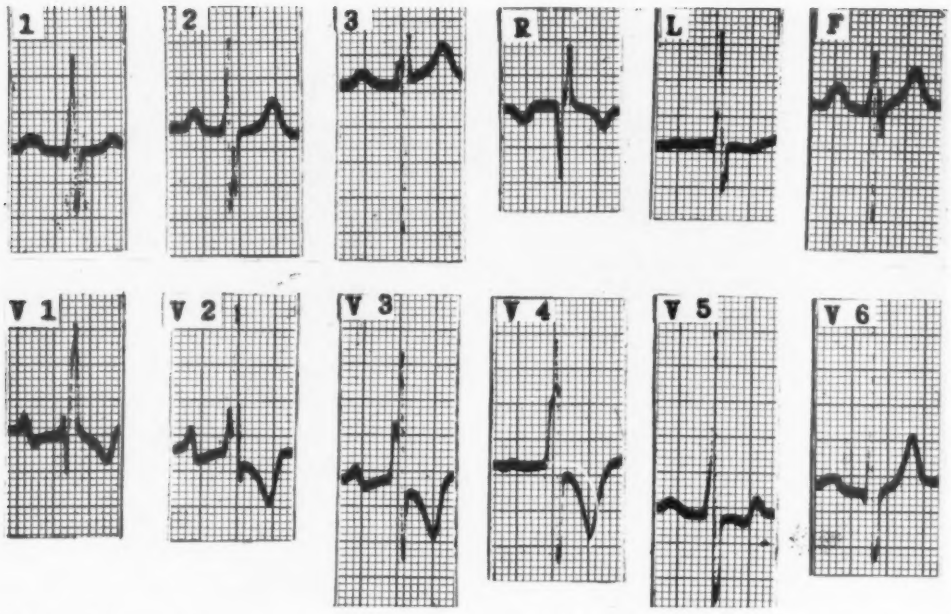


Fig. 8. Persistent common atrioventricular canal. Peaked, tall P waves in V_1-V_2. Wide P waves in lead 1, V_5-V_6. Combined atrial overloading.

pretation of the electrocardiograms and their correlation with the hemodynamic data lead us to the following conclusions:

(1) In three cases there was right atrial overloading and in two this overloading was of the combined type (right and left atria) (Fig. 7).

(2) The largest average of the amplitude of the P waves in this group, when compared with the series of cases of pulmonic stenosis and tetralogy of Fallot, probably depends upon the more pronounced degree of arterial desaturation found in these patients with complete transposition of the great vessels.

PERSISTENT COMMON ATRIOVENTRICULAR CANAL

We had 6 patients in this group. Four of them showed the complete type of this malformation, i.e., lack of fusion of the two atrioventricular endocardial cushions with each other and with the atrial and the ventricular septal complexes.[17] The other 2 had the incomplete form, i.e., atrial septal defect of the ostium primum type, with shortening of the anterior leaflet of the mitral valve, without interventricular communication. The ages of the patients varied from 15 months to 38 years.

SAP: It ranged from +45 degrees to +65 degrees in the frontal plane. In the horizontal plane it was pointing forward in 5 cases and parallel to the frontal plane in the other one.

Duration in the Limb Leads: It varied from 0.06 to 0.12 sec, the average being 0.09 sec.

Amplitude in the Limb Leads: The amplitude of the P wave ranged from 1 mm to 2.5 mm. The average was 1.8 mm.

Morphology in the Limb Leads: The P wave was slightly peaked in 4 cases and normal in 2.

Precordial Leads: Lead V_1: The P wave was entirely positive and peaked in 5 cases; in the other one it showed a plus-minus morphology,

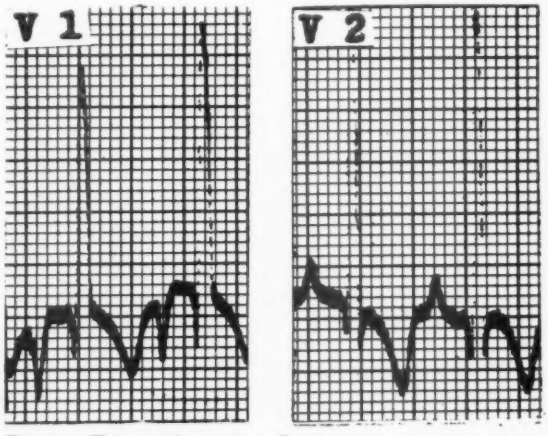


Fig. 9. Tricuspid atresia. P waves are negative, deep and narrow in V_1 and peaked and positive in V_2. Right atrial overloading. See text.

both areas of positivity and negativity being equal.

Lead V_2: In all cases the P waves were entirely positive, peaked and tall (1.5 mm or more). In 4 of the cases this peaking morphology extended to V_3.

Leads V_5 and V_6: The P waves were normal in 4 cases, and notched with increased duration (0.11 and 0.12 sec) in the other 2.

Index of Macruz: It was below 1.0 in 4 cases; between 1.0 and 1.6 in the other 2 cases.

Hemodynamic Correlation: The hemodynamic studies in this group demonstrated a left-to-right shunt at the atrial level in all cases. In 5 the magnitude of the shunt was above 60 per cent. In 4 patients there also existed a left-to-right shunt at the ventricular level. From the electrocardiograms we may conclude that there were signs of right auricular overloading in all cases, and in three of them associated left atrial overloading was very suggestive (Fig. 8).

TRICUSPID ATRESIA

Two children (5 and 7 months) having congenital tricuspid atresia were studied in this series. In both the diagnosis was confirmed by autopsy.

SAP: It was localized at +50 degrees pointing forward in one case, and at +40 degrees also pointing forward in the second patient. In this last case we considered the auricular vector as directed anteriorly, in spite of the fact that the P wave was entirely negative in lead V_1, although completely positive in V_2. Further considerations on this subject will be stressed later.

Duration in the Limb Leads: The P waves measured 0.07 second and 0.08 second, respectively.

Amplitude in the Limb Leads: The auricular waves measured 3.2 mm and 4 mm, respectively.

Morphology in the Limb Leads: The P waves in both cases were extremely peaked.

Precordial Leads: Lead V_1: In one case the P wave was entirely positive, peaked, measuring 2.5 mm in height; in the other case, the auricular wave was negative, deep (4.7 mm), and narrow (Fig. 9).

Lead V_2: In both cases the P waves were peaked and entirely positive, having an amplitude of 2.8 mm and 3.2 mm, respectively. This peaking morphology extended to V_5 and V_6 in the two cases.

Index of Macruz: It was 1.1 and 1.3, respectively.

EBSTEIN'S DISEASE

We had only one case in our series, a 16-year-old female presenting a moderate degree of cyanosis.

Analysis: The SAP was at +45 degrees pointing forward. In the limb leads the longest duration of the P wave was 0.08 sec, and the largest amplitude 2.2 mm. Morphologically, the auricular waves could be considered as normal. In lead V_1 the P waves were entirely positive, slightly peaked and measuring 2 mm in amplitude. In V_2 they also were completely positive, slightly peaked with an amplitude of 1.7 mm. In the left precordial leads the P waves were normal. The index of Macruz in this case was 0.6 (Fig. 10).

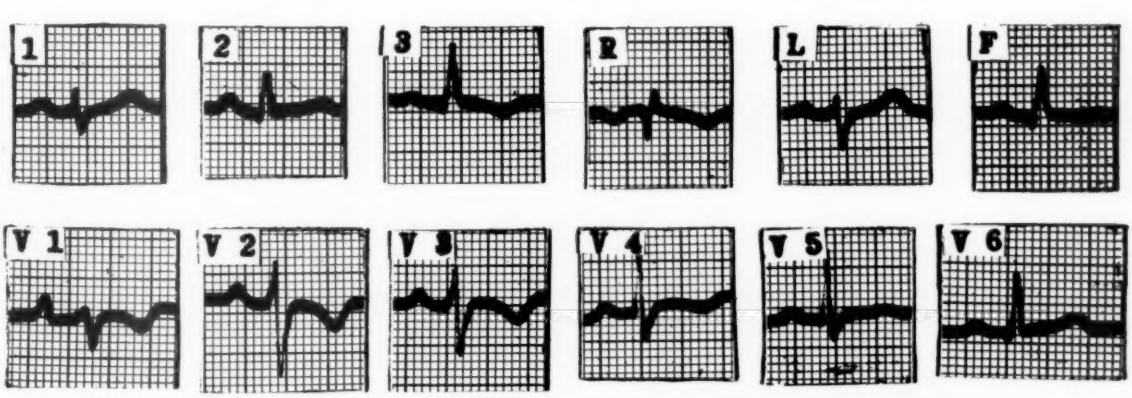


Fig. 10. Ebstein's disease. Peaked, tall P waves in V_1—right atrial overloading.

PULMONARY DISEASES

The electrocardiograms of 52 patients with chronic pulmonary disease were analyzed. All of them had well-characterized emphysema. In 18 cases this was complicated by cor pulmonale.

The ages of the patients varied between 28 and 50 years. Cases in which there was any evidence of cardiac diseases, such as coronary sclerosis, hypertension and aortic or mitral lesions, which could give rise to associated left auricular and ventricular overloading, were not included in this series.

Pulmonary Emphysema Without Cor Pulmonale (34 cases).

SAP: The auricular vector varied from +60 degrees to +100 degrees in the frontal plane (Fig. 11). In the horizontal plane it pointed forward in 25 cases, backward in 3, and was parallel to the frontal plane in 6 cases.

Duration in the Limb Leads: It ranged from 0.08 sec to 0.10 sec, the average being 0.085 sec.

Amplitude in the Limb Leads: It varied from 1.2 mm to 2.6 mm. The average was 2.2 mm.

Morphology in the Limb Leads: The auricular wave was peaked in 32 cases (97 per cent), and normal in 2 cases.

Precordial Leads: Lead V_1: In all patients a plus-minus complex was seen. The positive area was larger than the negative one in 25 cases, smaller in 3 cases, and in 6 cases both areas were equal. In the three cases in which there existed a predominant negative phase, this part of the P wave was not as large as that found in cases of left atrial overloading. In left precordial leads, the P waves were normal.

Pulmonary Emphysema With Cor Pulmonale (18 Cases)

SAP: It varied from +65 degrees to +110 degrees in the frontal plane (Fig. 11). As one can see in this figure, there is a tendency of the auricular vector to be deviated more to the right in these cases than in those of emphysema without cor pulmonale.

In the horizontal plane, it was pointing forward in 15 cases and parallel to the frontal plane in the other 3 cases.

Duration in the Limb Leads: It varied between 0.08 and 0.11 sec. The average was 0.092 sec.

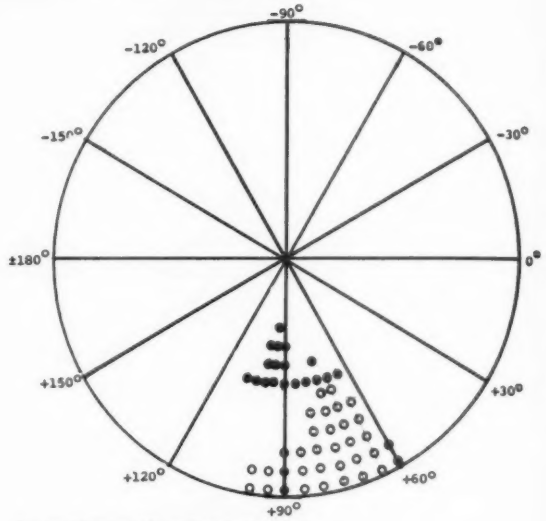


Fig. 11. The distribution of the P vector in the frontal plane in 34 cases of pulmonary disease without cor pulmonale and in 18 cases with cor pulmonale. See text.

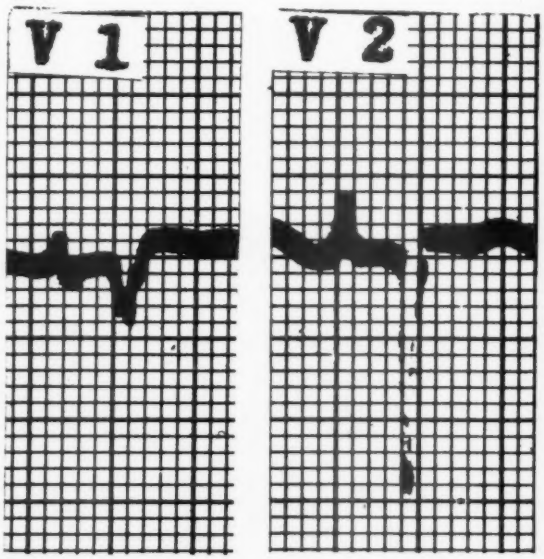


Fig. 12. Cor pulmonale. Tall, peaked P waves in V_1-V_2. See text.

Amplitude in the Limb Leads: It ranged from 2 to 3 mm, the average being 2.7 mm.

Morphology in the Limb Leads: The P waves were peaked in lead 2, lead 3, and aVF in all cases.

Precordial Leads: In 13 patients a plus-minus isodiphasic P wave was present in V_1, with pre-

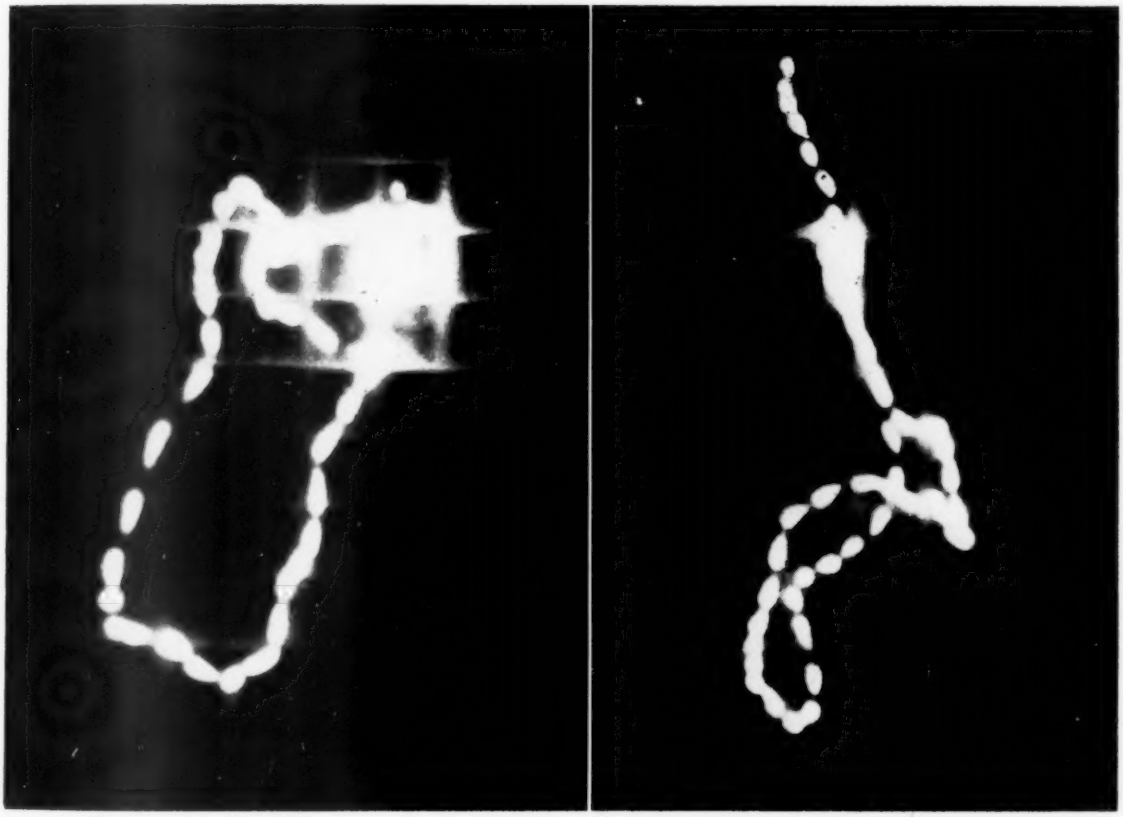
dominance of the area of positivity. In the other 5 the P wave was completely positive and peaked, not only in V_1 but also in V_2 (Fig. 12). In the left precordial leads (V_5 and V_6), they were normal in 15 cases and peaked in 3 cases.

VECTORCARDIOGRAPHIC STUDY

We have performed a vectorcardiographic analysis in 20 of the patients discussed.

Mitral Lesions—10 Cases: The P loop was oriented to the left and posteriorly in all cases. It showed a counterclockwise rotation in the frontal and horizontal planes and a clockwise rotation in the sagittal one. The loop was wider than normal in 8 of the patients and an eight-shaped figure was found in four cases. Special attention was paid to the localization of the mean vector calculated from the P loops in the sagittal plane (Figs. 13 and 14). It ranged from +95 degrees to −140 degrees. Figure 15 shows the distribution of the mean auricular vector in this plane.

Congenital Heart Disease—10 Cases: Dissected P loops were analyzed in 10 patients presenting congenital malformation. These consisted of the following: interatrial septal defects (ostium secundum type)—4; persistent common atrioventricular canal—2; pure pulmonic stenosis—2, tetralogy of Fallot—1; and Ebstein's disease—1. All cases of interatrial septal defect had a shunt flow above 65 per cent and showed tall peaked P waves in leads V_1 and V_2. The patients with pulmonic stenosis, tetralogy of Fallot and Ebstein's disease had right atrial systolic pressures above 10 mm Hg. The two cases of persistent atrioventricular canal showed high



13 14

Fig. 13. Mitral stenosis. Isolated P loop in the sagittal plane. The loop is wide, clockwise rotated with backward orientation (+100°).

Fig. 14. Mitral stenosis. The isolated P loop in the sagittal plane shows clockwise rotation, an eight-shaped figure and is localized at +110° approximately (backward orientation).

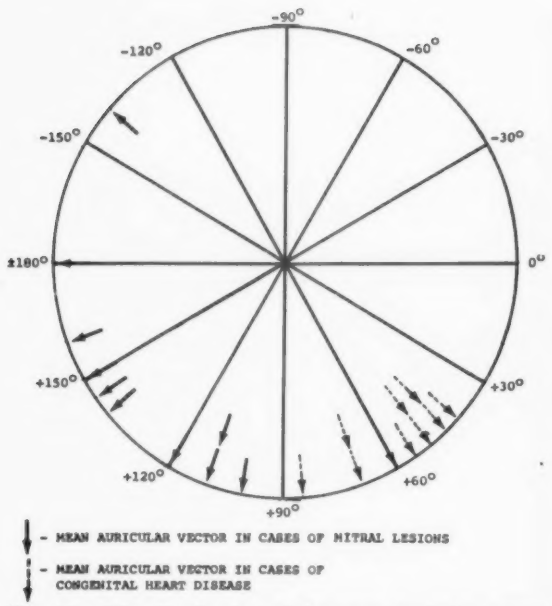


Fig. 15. The distribution of the mean auricular vector in the sagittal plane, as calculated from the vectorcardiogram in patients with mitral lesions and congenital cardiac malformations.

pressures in the right atrium, and electrocardiographic signs of combined auricular overloading were present in one of them.

In all these 10 patients, the direction of the inscription of the P loop was similar to that found in cases of mitral disease, i.e., counterclockwise rotation in the frontal and horizontal planes and clockwise rotation in the sagittal one. Although the localization of the mean auricular vector, calculated from the P loop in the sagittal plane, was completely different, it pointed forward in all cases, ranging from +40 to +85 degrees (Fig. 15). The loops showed a normal width, but the magnitude was increased in contrast to what one sees in cases of left auricular overloading (Fig. 16). We did not find any particular difference among the types of congenital malformations studied in this series as far as the vectorcardiogram was concerned.

Discussion

LEFT AURICULAR OVERLOADING

The left atrium may be overloaded in many conditions. Electrocardiographic signs of increased electrical activity, as a consequence of dilatation or hypertrophy of this chamber, are frequently found in those situations which pro-

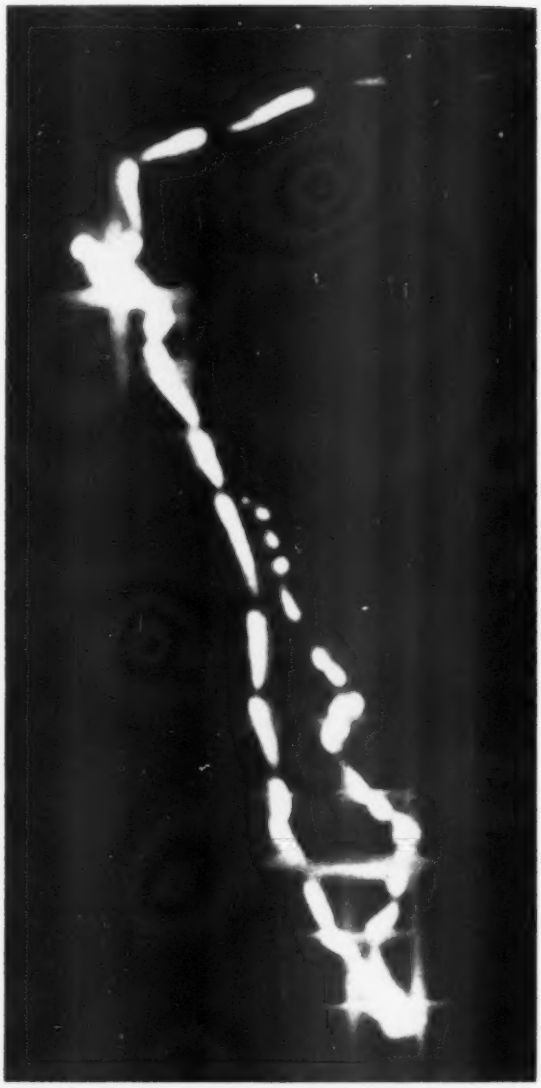


Fig. 16. Pulmonic stenosis. Isolated P loop in the sagittal plane, showing increase in magnitude and forward orientation. See text.

duce left ventricular overloading: systemic hypertension, aortic stenosis, coarctation of the aorta, patent ductus arteriosus, and arteriosclerotic heart disease with enlarged left ventricle. P wave changes suggesting left atrial overloading are also found in acute distentions of this chamber during acute pulmonary edema.[18] However, the most typical conditions which give rise to left auricular overloading are the mitral lesions—stenosis, insufficiency or both.

Orientation of P Vector: The most constant electrocardiographic finding we have noticed in

our series concerning left auricular overloading was a marked backward orientation of the P vector, which is expressed in the record by a pronounced predominance of the area of negativity of the P wave in lead V_1. In the frontal plane the mean auricular vector lies generally between +60 degrees and −10 degrees. In some cases of pure mitral stenosis with vertical heart[19] one may find the AP with a tendency to deviate to the right (beyond +65 degrees). However, we feel that in these cases an associated right atrium overloading must be ruled out, since in our series, all patients in whom the AP showed such a tendency to rightward deviation also had increased right auricular pressures.

Morphology of P: The typical morphology of left auricular overloading in the right precordial leads (V_3R and V_1) is characterized by an initial positive deflection of small amplitude, followed by a negative one, deeper and larger. This second phase expresses the delayed activation of a dilated and/or hypertrophied left atrium.

In 6 of our patients the P wave was completely negative in V_1 (Fig. 17). It is worthwhile to stress that in all these 6 cases the existence of an extremely dilated left atrium was demonstrated during the surgical procedure.

Duration of P: Another fact that we would like to point out here is the duration of the P wave in the limb leads. It has been generally accepted that in left atrium overloading this

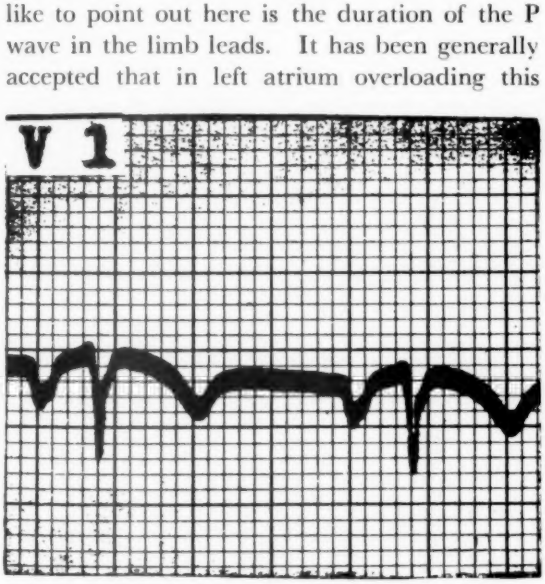


Fig. 17. Mitral stenosis. Completely negative P waves in lead V_1. An extremely dilated left atrium was demonstrated in this case during the surgical procedure.

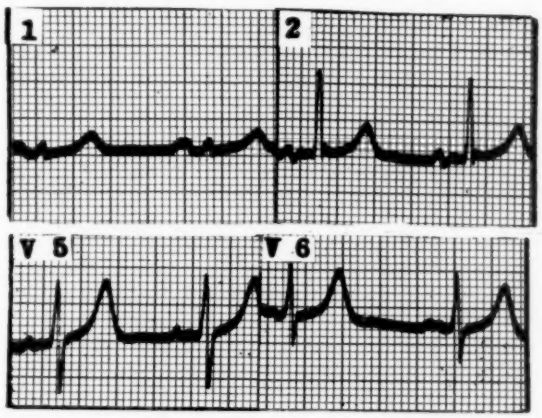


Fig. 18. Mitral stenosis. Diphasic notched P waves in leads 1 and 2, V_5-V_6, suggestive of left atrial overloading.

duration must exceed 0.10 sec. In 7 of our patients with mitral stenosis, the duration of the P wave was 0.09 sec. All of them showed hypertrophied left atria at surgery; these however, were not significantly dilated. This leads us to conclude that if there are other electrocardiographic signs of left auricular overloading, such as diphasic P waves and leftward and backward deviation of the P vector, this diagnosis may be considered even if the duration of the P wave is only 0.09 sec. In 14 patients the duration of the P wave was equal to or more than 0.12 sec. All of them had very enlarged left atria. Thus we concur with Reynolds[20] who demonstrated that the longer the duration of the P wave, the more dilated is the left atrium.

Increase in duration of the P wave in V_5-V_6 (0.10 sec or more) has been a constant finding in left atrial enlargement.

Shape and Height of P: The shape of the P wave is also an important sign for the diagnosis of left atrium overloading. Diphasic notched P waves, particularly in lead 1, lead 2, and V_5-V_6, strongly suggest left atrium involvement (Fig. 18).

The augmented voltage of the P wave in the limb leads has been related to right atrium overloading. We have also found this an accurate sign for such a diagnosis. However, in some instances one may have an increase in the amplitude of the second part of a diphasic P wave, in cases with a normal right atrium. These patients actually have markedly hyper-

trophied left atria. This is easy to understand since we know that the second part of the P wave represents the activation of the left atrium. Whenever the higher part of the wave is the first one, the hypertrophy is localized in the right atrium.

Vector P Loops: The vectorcardiogram gives us useful information in many cases, by demonstrating the leftward and backward orientation of the P vector, as well as by showing the deformity of the auricular loop, which becomes wider than normal, acquiring in a few cases an eight-shaped figure.

In comparing our cases of pure mitral stenosis, pure mitral insufficiency and both as combined lesions, we could not demonstrate any difference among them, as far as the P wave and P vector were concerned. However, the differential diagnosis between mitral stenosis and insufficiency may be suggested by the absence or presence of signs of associated left ventricular overloading.

RIGHT AURICULAR OVERLOADING

From the hemodynamic viewpoint, the right auricle is considered as being overloaded either by an increase in pressure or by an augmented volume of blood in this chamber (systolic and diastolic overloadings). In some instances both situations may coexist.

Increase in pressures in the right atrium generally appears either as a consequence of an augmented right ventricular pressure or on account of congenital and acquired defects of the tricuspid valve. The first group would include all cases of disease of the lungs and mitral lesions complicated by pulmonary hypertension, pulmonic stenosis, tetralogy of Fallot, transposition of the great vessels, truncus arteriosus, patent ductus arteriosus and interventricular septal defects (with pulmonary hypertension), Eisenmenger complex, etc. Functional tricuspid insufficiency seems to play an important role in the development of the right auricular overloading in many of these cases. In the second group, one would have patients with tricuspid stenosis and atresia, organic tricuspid insufficiency and Ebstein's disease.

Augmented volume of blood to the right atrium is found in the presence of interatrial septal defects and anomalous pulmonary venous drainage. In some of these cases there also exists increased right atrial pressure.

Depending upon the degree of the above-mentioned hemodynamic changes, dilatation and/or hypertrophy of the right atrium may occur, thus giving rise to the appearance of the electrocardiographic signs suggestive of right auricular overloading. However, it must be stressed here that the criteria for the diagnosis of right auricular overloading are not as well defined as those for left atrium overloading. Other factors influence the P wave and the P vector, and many times they may simulate the patterns that one sees when the right auricle is hypertrophied and/or dilated. Arterial desaturation found in patients with right-to-left shunts or chronic pulmonary diseases gives rise to peaked, tall P waves similar to those seen in right atrial hypertrophy. Pulmonary emphysema, by producing vertical position and dextrorotation of the heart, brings the P vector to the right even in the absence of any overloading of the right auricular chamber.

Nevertheless, based on our own experience and those of other authors,[6,13,21,22] we feel that some conclusions may be reached concerning the electrocardiographic diagnosis of right auricular overloading. For the sake of convenience we will discuss separately the groups of congenital heart diseases and pulmonary diseases.

Congenital Heart Disease

Amplitude and Configuration of P: The amplitude of the P waves in the limb or in the precordial leads was above 2 mm in all cases in which the systolic pressures in the right atrium were equal to or more than 10 mm Hg. Patients with both elevated right auricular pressures and arterial desaturation (right-to-left shunts) presented the highest P waves. Such a fact was well demonstrated in our series of tetralogy of Fallot, transposition of the great vessels and tricuspid atresia. Peaked P waves in the limb leads, precordial leads or both were a constant finding whenever right atrium overloading was present.

In those cases in which the right auricular pressures were below 10 mm Hg, as for instance in the majority of cases of interatrial septal

defect and in some cases of pulmonic stenosis, tetralogy of Fallot and persistent common atrioventricular canal, although the amplitude of the P waves was below 2 mm these waves showed a typical peaking morphology, particularly in V_1 and V_2. In atrial septal defects and persistent common atrioventricular canal, this morphology seems to depend upon the degree of the overloading produced by the left-to-right shunt. This led us to conclude that slight degrees of right auricular overloading may exist, even in the presence of P waves considered to be of normal amplitude from the established criteria.

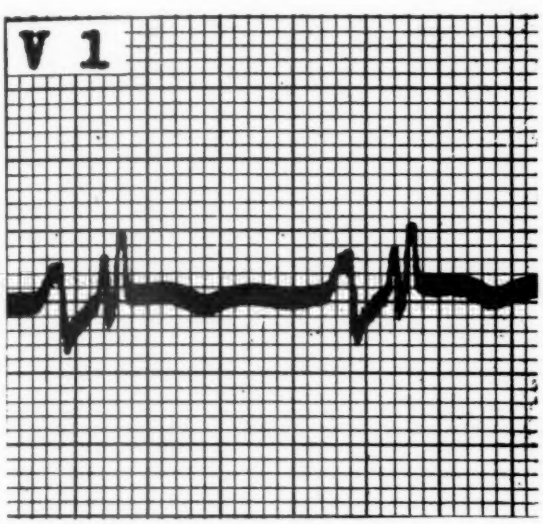


Fig. 19. Tricuspid atresia. Diphasic, tall P waves in V_1 showing a "fast intrinsicoid deflection between two acuminated vertices." This is considered as meaning right atrial overloading. See text.

The duration of the P waves remained within normal limits, when no associated left atrium overloading existed.

P in V_1 and V_2: In the majority of our cases of right auricular overloading, we found entirely or predominantly positive tall peaked P waves in lead V_1. In a few patients this lead had diphasic, tall P waves, showing what Cabrera[19] has described as "a fast intrinsicoid deflection between two acuminated vertices" and considered as meaning right auricular hypertrophy (Fig. 19).

In one of our patients with tricuspid atresia, we found in lead V_1 a negative deep P wave which returned to the isoelectric line by means of a fast upward segment (Fig. 9). This morphology has been described by Puech[6] as extremely rare and representing right auricular hypertrophy. We feel that in such cases, as a consequence of a forward and slight leftward rotation of a very enlarged right atrium, the direction of the atrial vectorial forces points away from V_1. In such a situation V_2 probably becomes the real perpendicular projection of the auricular electric center (rotation of the sino-auricular node forward and to the left), the P waves being tall, peaked and entirely positive in this lead, as happened in our case. This peculiar negative pattern of the P wave in lead V_1 could simulate the morphology described in patients with mitral lesions, in which the negative phase of the P wave generally predominates. However, in left auricular overloadings, this negative phase is wide and one does not find in lead V_2 the positive atrial waves as those referred to above.

The presence of positive, tall (above 1.5 mm), peaked P waves in lead V_2 was a very constant finding in our patients in whom right auricular overloading existed. In those cases in which cyanosis was present, the average of the amplitude of the P waves was higher than in the non-cyanotic group. In the left precordial leads the auricular waves showed a normal pattern in the majority of the cases; however, in a few patients they were peaked in V_4, V_5, and V_6.

Mean Auricular Vector: The mean auricular vector was localized in the great majority of the cases between +30 degrees and +60 degrees in the frontal plane, which explains the larger amplitude of the P waves in lead 1 than in lead 3. This is in agreement with the findings of Zuckermann[13] who described what he called the "P congenitale": tall, peaked P waves in the limb leads with the auricular vector in intermediate or semihorizontal positions. In the horizontal plane, in almost all patients, the mean axis of atrial activation was pointing forward.

In 65 per cent of those cases in which right auricular overloading existed as an isolated condition (no left atrium involvement), the index of Macruz was positive for such a diagnosis.

Ventricular Complex in Right Atrial Overloading:

In judging the existence of right atrial overloading, the analysis of the ventricular complex may give us important information, as far as congenital heart lesions are concerned. Thus in presence of a divergence between the auricular and ventricular axes (AP to the right and AQRS to the left), the diagnosis of right auricular overloading is very suggestive. Although, in some cases, the amplitude and morphology of the P waves may not be very significant, the existence in the same record of typical right ventricular hypertrophy permits the suggestion of an associated right auricular overloading. A QR pattern of the ventricular complex in lead V_1 has been described as meaning dilatation of the right auricle and it has been frequently found in patients with Ebstein's disease.[12] In our series we found such a morphology in six cases (Fig. 20).

The vectorcardiogram is also a useful complementary method. P loops with normal width, increased magnitude and a forward orientation are very suggestive of right atrial hypertrophy.

Pulmonary Diseases

It seems to be fairly well established by now that diseases of the lungs may produce changes in the P wave and the P vector, because of three factors:

(1) *By Changing the Anatomic Position of the Heart in the Chest:* The heart is dextrorotated, vertical and displaced posteriorly. This is expressed in the ECG by a tendency to rightward deviation of the QRS and P vectors, "S_1, S_2, S_3" pattern. The main factor responsible for these changes is the pulmonary emphysema.

(2) *By Hypoxia:* As a result of disturbance in the phenomenon of hematosis there exists arterial desaturation, the P waves becoming tall and peaked. The mechanism of this is not well understood.

(3) *By Right Atrial Overloading:* Pulmonary hypertension gives rise to right ventricular hypertrophy and dilatation (cor pulmonale). In some cases, particularly if functional tricuspid insufficiency appears or if right ventricular failure develops, the right atrium becomes overloaded. This is electrically represented by tall and peaked P waves.

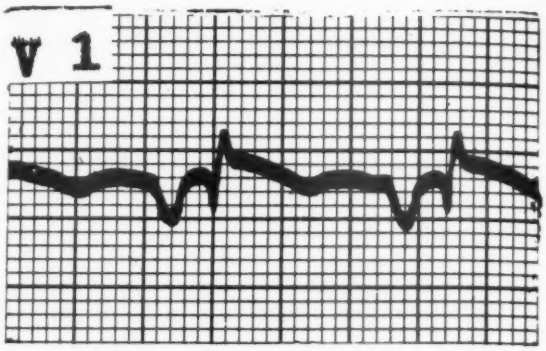


Fig. 20. QR pattern in V_1 suggesting right auricular dilatation. See text.

The above-mentioned factors may exist independently or combined.

In cases of acute pulmonary affections, for example during the crisis of bronchial asthma, the major factor involved is hypoxia. The P waves become peaked and increased in voltage, while the P vector shows a slight tendency to deviate to the right. No changes in the QRS complex appear, demonstrating the absence of alteration in the position of the heart in the chest. These changes are transitory, disappearing as the patient recovers.

In chronic pulmonary diseases complicated by emphysema, two of the factors—changes in the position of the heart and hypoxia—are present.

Finally, when these conditions give rise to decompensated cor pulmonale or to functional tricuspid insufficiency, all of these factors exist.

Mean Atrial Vector: The most striking finding as far as the auriculogram is concerned, for the diagnosis of pulmonary disease has been the localization of the mean atrial vector in the frontal plane. The P axis was always found in our series deviated to the right (beyond +60 degrees). In the horizontal plane the auricular vector generally points forward, although in many instances it may be backward or parallel to the frontal plane. In both limb and precordial leads, the P waves were peaked in 99 per cent of the cases and their amplitude was above 2 mm in the great majority of the patients.

In the presence of pulmonary emphysema, it seems to be very difficult to decide by the auriculogram whether or not there also exists right auricular overloading. In 34 of our patients, the heart had a normal size, the

venous pressure was within normal limits and no clinical evidence of cor pulmonale was detected. In the other 18, the right chambers were enlarged and the venous pressure was elevated. No conclusive electrocardiographic differences concerning the auriculogram could be established between the two groups (with and without cor pulmonale). We have, however, noticed a tendency of the P vector to be more deviated to the right as well as larger amplitudes of the P waves in the series of patients with definite cor pulmonale.

COMBINED AURICULAR OVERLOADING

Combined auricular overloading may occur in many conditions. The most common are: (1) associated mitral and tricuspid lesions, (2) Lutembacher's syndrome, (3) persistent common atrioventricular canal, (4) trilogy of Fallot, (5) pentalogy of Fallot, (6) tricuspid atresia with interatrial septal defect, and (7) Ebstein's disease.

In the first two conditions, the electrocardiographic signs suggesting the combined overloading are present in almost all cases. In the other affections, those signs are not very frequent, since as a consequence of a marked predominance of the right over the left atrium, the auriculogram only suggests in the majority of cases right auricular overloading.

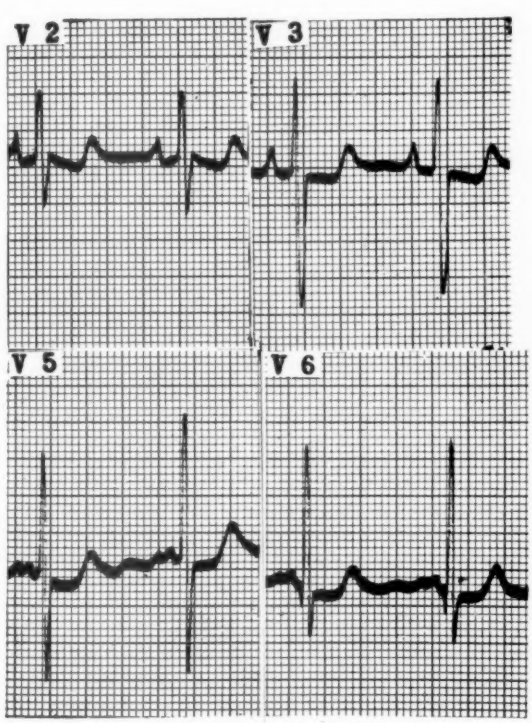


Fig. 21. Persistent common atriovetnricular canal. Tall, peaked P waves in right precordial leads and wide, notched P waves in V_5-V_6. This type of combination is very suggestive of biatrial overloading.

Diagnosis of Combined Atrial Overloading: The existence of a combined atrial overloading may be suspected from the electrocardiogram for two reasons: (1) The presence of morphologic signs compatible with overloading of both atria:

(a) Increase in the amplitude and in the duration of the P waves in the limb leads. This was seen in two of our cases of transposition of the great vessels as well as in two cases of atrioventricularis communis.

(b) The existence of peaked P waves in the right precordial leads and large, notched P waves in the limb leads and/or in V_5-V_6. This type of combination was also seen in the same patients referred to before (Fig. 21).

(c) Isodiphasic auricular waves in V_1, the positive phase being tall and peaked, and the negative area deep and wide. We have seen this type of wave in one patient with both mitral and tricuspid rheumatic stenosis.

(2) The existence of morphologic signs of left atrial overloading associated with a tendency of the AP to deviate to the right. We found this combination in 7 of our patients with mitral stenosis. Two of them also had rheumatic tricuspid stenosis and the other five, functional tricuspid insufficiency (Fig. 2).

The opposite, i.e., morphologic signs of right auricular overloading associated with a tendency of the P vector to deviate to the left, cannot be considered as an index of combined atrial overloading, since in many cases of congenital heart disease, even in the absence of left auricular overloading, the AP may be found about +20 or +10 degrees, on account of the horizontal position of the atria in these malformations.

SUMMARY

The authors studied the auriculograms of 193 patients presenting mitral lesions (41 cases), congenital cardiac malformations (100 cases), and pulmonary disease (52 cases). In the great majority of the cases hemodynamic correla-

tions were established and in 20 patients the vectorcardiogram was analyzed.

The chief characteristics of the P wave and the P vector in left, right, and combined atrial overloading are stressed.

The following conclusions are drawn:

(1) The most important findings for left atrial overloading are a marked backward orientation of the P vector, appearance of notching and increase in the duration of the P waves in the limb and left precordial leads.

(2) There seems to exist a correlation between the duration of the P waves and the degree of left atrial dilatation.

(3) P waves with normal duration may exist in the presence of hypertrophied but not significantly dilated left auricles.

(4) A tendency of the AP to deviate to the right in patients with mitral lesions was found whenever the right auricular pressures were elevated.

(5) In all cases of significant right auricular systolic overloading (systolic pressure above 10 mm Hg) in our series of congenital heart diseases, the amplitude of the P waves was above 2 mm either in the limb or precordial leads.

(6) Arterial oxygen desaturation tends to increase the amplitude of the P waves. Patients with both elevated right atrial pressures and arterial desaturation presented the highest P waves in this study.

(7) Slight degrees of right atrial overloading, particularly in patients with interatrial septal defect, were detected in many cases by the presence of peaked P waves of normal amplitude, mostly in V_1 and V_2.

(8) The interpretation of the ventricular complex adds important data in the diagnosis of right atrial overloading.

(9) Pulmonary emphysema and arterial desaturation as a consequence of disturbance in the mechanism of hematosis, in patients with chronic disease of the lungs, produce marked changes in the P waves and the P vector. The P waves become tall and peaked and the AP is deviated rightward and downward.

(10) In the presence of pulmonary emphysema with arterial desaturation, it is very difficult to decide by the auriculogram whether there also exists right auricular overloading.

(11) The existence of combined auricular overloading may be suspected from the ECG for two reasons: (a) the presence of morphologic signs compatible with overloading of both atria; (b) the existence of morphologic signs of left atrial overloading associated with a tendency of the AP to deviate to the right.

(12) Vectorcardiogram: P loops with leftward and backward orientation, increased in width, and sometimes showing eight-shaped figures are very suggestive of left atrial overloading. P loops with normal width, increased magnitude and a forward orientation are diagnostic of right atrial overloading.

Acknowledgment

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Ventricular Endocardial Leads in Left Bundle Branch Block and Left Ventricular Hypertrophy

Correlation with the Vectorcardiogram and Electrocardiogram*

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THE difficulty in differentiating left bundle branch block from left ventricular hypertrophy by means of the standard electrocardiogram is well known. Any method which can contribute to this differentiation or to the evaluation of proposed criteria is to be desired. The introduction of left heart catheterization[1] and combined heart catheterization[2] provides a method to study septal activation in humans and its deviations from the normal, and to correlate these findings with the peripheral electrocardiogram. This study was undertaken in particular to evaluate equivocal tracings and suggested current electrocardiographic criteria for left bundle branch block.

MATERIAL AND METHODS

Thirty-one patients with acquired heart disease were studied. The electrocardiographic tracings were analyzed for evidence of left ventricular hypertrophy according to the criteria of Sokolow and Lyon,[3] Wilson and associates[4] and Goldberger.[5] The criteria for incomplete left bundle branch block were those of Barker,[6] Sodi-Pallares and associates,[7] and Wilson and associates,[4,8] and for complete left bundle branch block those of Barker[6] and Wolff.[9] In addition, vectorcardiograms were obtained in 13 patients and examined for left bundle branch block according to the criteria of Grishman.[10]

Endocardial tracings were obtained by left heart catheterization or combined heart catheterization, procedures which have been previously reported.[1,2] The right heart Cournand electrode catheter was positioned with guidance by fluoroscopy and by pressure tracings in the pulmonary artery, right ventricular outflow tract, right ventricular mid and tricuspid areas, and low right atrium. Following placement of the 17-gauge left heart catheterization needle in the left atrium, a specially constructed polyethylene catheter containing a fine German-silver wire exposed only at the distal tip was maneuvered into the left ventricle. Tracings were obtained in the left ventricle and left atrium, and simultaneously in the left ventricle and right ventricle. The position of the left heart catheter could not be ascertained fluoroscopically but was judged to be in the left ventricle by the occurrence of ventricular premature beats, ventricular current of injury deflections, and by changes in the voltage and configuration of the P and QRS endocardial complexes from the left atrium (Fig. 1).

For convenience in analyzing the data, the patients were divided into the following groups based on the electrocardiographic diagnosis. The clinical diagnosis was confirmed by cardiac catheterization in all patients and cardiac surgery in the majority. *Group I* includes 14 patients with evidence of left ventricular hypertrophy. The diagnoses were aortic stenosis in nine, aortic stenosis and mitral stenosis in three, in whom the mitral stenosis was minor in one patient, and essential hypertension and coronary artery disease in one. Aortic stenosis and pulmonic stenosis were present together in one patient. *Group II* includes 5 patients with left ventricular hypertrophy and associated incomplete left bundle branch block. The diagnoses were aortic stenosis in four and aortic insufficiency in one. *Group III* consists

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of 2 patients who showed equivocal findings presenting slurring in leads facing the left ventricle without other criteria for incomplete left bundle branch block. T wave abnormalities due to digitalis were also noted. The clinical diagnoses were severe aortic stenosis in one and severe aortic stenosis and mitral stenosis in the other. *Group IV* comprises 2 patients with complete left bundle branch block. The diagnoses were major aortic insufficiency and minor aortic stenosis in one, and coronary artery disease in the other. *Group V* consists of 8 patients without left ventricular hypertrophy or left bundle branch block. Five had T wave abnormalities which were due to digitalis administration in three. The diagnoses were minimal and moderate aortic stenosis in three, and minor aortic stenosis and mitral stenosis in two. Two patients had left atrial hypertrophy and mitral stenosis. One patient had right bundle branch block and mitral regurgitation.

Results

Group I. Left Ventricular Hypertrophy: In 10 patients in this group a QS pattern was recorded in the left ventricle (Fig. 2*a*). In 6 of these same patients an rS was observed in the right ventricle (Fig. 3A). Absence of q-V_6 was noted in 4 patients. In V_1 the r deflection was present in all, but was less than 1 mm in 5. Correlation of the endocardial S-T segment with the peripheral V_6 S-T segment was variable, being elevated in the left ventricle in 7, and normal or depressed peripherally. The T wave in the endocardial lead and in V_6 were opposite in direction in the majority of patients, and were upright in the left ventricle. Vectorcardiograms obtained in five patients were consistent with left ventricular hypertrophy in 4 and T wave abnormality in one. However, a figure-of-eight loop in the horizontal plane was noted in one of the former.

In 4 patients in this group (Table I, cases 2–5) the left ventricular endocardial patterns were variable and were those of an rS in two (Fig. 3B), qR in one, and QR in one (Fig. 2*b*). Two types of complexes were observed in one patient. A right ventricular lead was recorded in one patient (case 3) and showed a QS deflection. In this group absence of q-V_6 was

TABLE I

Patients with Left Bundle Branch Block Diagnosed by the Endocardial Lead

Case number	ECG diagnosis	VCG diagnosis	Endocardial lead				Precordial lead						
			LV pattern	LV S-T segment	LV T wave	RV pattern	r-V_1	q-V_6	Slurring*	qRS duration (sec)	VAT (sec)	S-T segment	T wave
1	LVH + ILBBB	LBBB	rS qRS	↑ ↓	↓ ↑	—	0	0	0	0.07	0.03	N	↓
2	LVH	LVH	rS	↑	↑	—	+	0	0	0.08	0.05	Slightly ↓	↓
3	LVH	—	rS	↑	↑	QS	0	0	0	0.07	0.05	Slightly ↓	↓
4	LVH	—	qR	N	↓	—	+	0	0	0.11	0.05	N	D
5	LVH	LVH	QR	Slightly ↑	D	—	+	+	0	0.07	0.03	N	D
6	CLBBB	LBBB	RR's	N	↓	—	0	0	R*nt*	0.16	0.12	N	↓
7	LVH + ILBBB	LBBB	qRS	↑	↑	—	0	0	+	0.10	0.06	↓	↓
8	DIG effect	—	qRs	N	↓	—	+	+	0	0.05	0.02	N	↓
9	LVH + ILBBB	—	—	—	—	QS	0	0	+	0.08	0.05	Slightly ↓	↓
10	LVH + ILBBB	—	qrS QS*sl*	N	↑	rS QS	+	0	+	0.10	0.04	↓	↓

LV—left ventricle. RV—right ventricle. *—slurring in leads facing the left ventricle. VAT—ventricular activation time. LVH—left ventricular hypertrophy. ILBBB—incomplete left bundle branch block. CLBBB—complete left bundle branch block. N—normal. D—diphasic. *nt*—notched. DIG—digitalis. *sl*—QS with slurring on the descending limb.

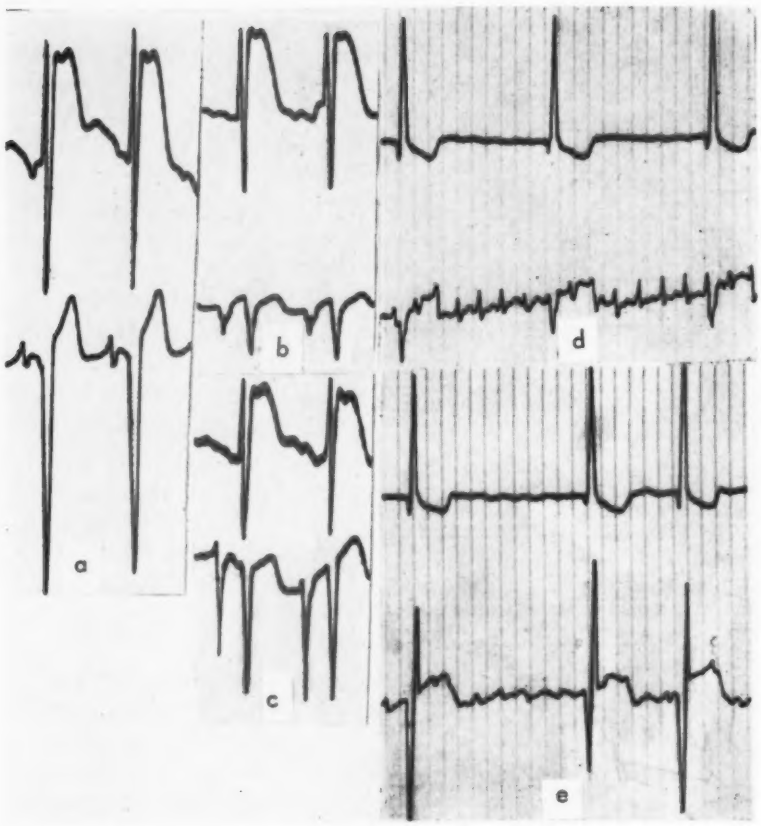

Fig. 1. Differences between the voltage and configuration of the left ventricular QRS pattern (*a* and *e*) and the left atrial QRS pattern (*b*, *c*, and *d*). Endocardial tracings below. Right ventricular tracing above in *a*, *b*, and *c*; V_6 above in *d* and *e*. Note the f waves in the left atrium in (*d*) which are only indistinctly seen in the left ventricle of this same patient in (*e*).

noted in all but one patient. The r-V_1, however, was present in three and absent in one. The S-T segments were normal and elevated in the left ventricle and normal and slightly depressed in V_6. The T waves were variable. Vectorcardiograms performed on two patients were consistent with left ventricular hypertrophy, although figure-of-eight loops were noted in the horizontal plane in both.

Group II. Left Ventricular Hypertrophy and Incomplete Left BBB: The left ventricular endocardial complexes obtained in 4 patients were variable and showed a qRS in one (case 7, Fig. 4A), QS in one, rS and qRS in one (case 1), and qrS and QS with slurring on the downward limb in another (case 10). In the latter patient a right ventricular lead likewise recorded two complexes, an rS in the outflow and tricuspid areas and a QS in the mid-position. Following aortic commissurotomy in this patient only a QS deflection was recorded in the right ventricle. In the fifth patient (case 9) only a right heart catheterization was performed and a QS was observed throughout the right ventricular cavity. In all 5 patients a q deflection was absent in V_6. However, r-V_1 was absent in 3, present in one, and present but minute in another. In all patients slurring of the upstroke of the R wave was present in leads facing the left ventricle. The S-T segments and T waves varied in a manner similar to the previous group.

Vectorcardiograms were obtained on 2 patients and suggested left bundle branch block in both by the posterior and leftward position of the loops and initial forces. Both were not typical, however, according to proposed criteria, since counterclockwise rotation in the horizontal plane was observed in 1 (case 1) and conduction delay was not definitely noted in the other (case 7).

Group III. Atypical QRS with Slurring: These two patients were of interest since their electrocardiograms were difficult to interpret, showing definite slurring in leads facing the left ventricle without other criteria for left

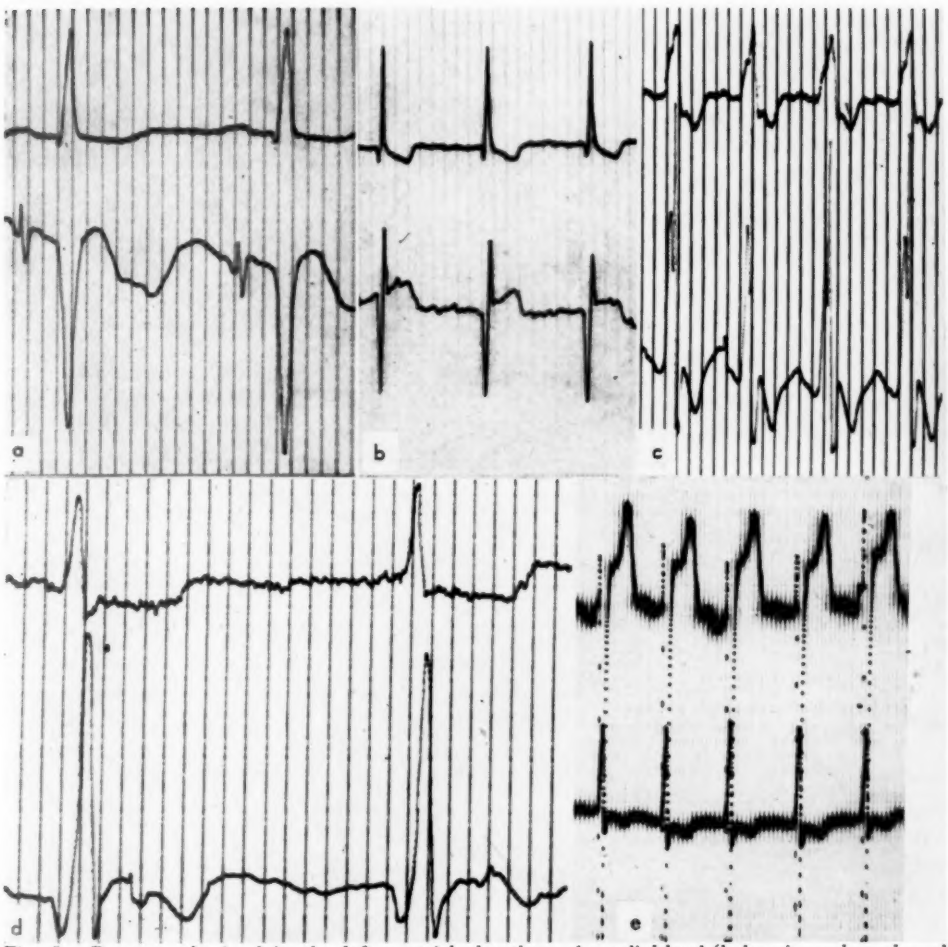

Fig. 2. Patterns obtained in the left ventricle by the endocardial lead (below in *a*, *b*, *c*, *d*, and above in *e*). V_6 above in *a*, *b*, *c*, *d*, and below in *e*. Time lines 0.04 sec in *a*, *d*, and *e*, and 0.1 sec in *b* and *c*. Paper speed 25 mm/sec in *b*, *c*, and *e*, and 75 mm/sec in *a* and *d*.

bundle branch block. Absence of the q-V_6 was noted in both while r-V_1 was present in one and absent in the other. A QS with slurring on the downward limb was recorded in the left ventricle in one. The S-T segments and T waves were elevated and diphasic respectively in the left ventricle, and normal and upright in V_6. In one patient only a right heart endocardial lead was recorded which showed an RS pattern. Although these findings are not in keeping with left bundle branch block in either case, they do not exclude the diagnosis, as will be discussed below.

Group IV. Complete Left Bundle Branch Block: In one patient only a right heart catheterization was performed and an RS was recorded in the right ventricle. This was an unexpected finding and one that is difficult to interpret.

In the other patient (case 6) a left heart catheterization was performed. An RR′S was recorded in the left ventricle (Fig. 4B). The R′ deflection occurred synchronously with the R of V_6. Both the endocardial and peripheral (V_6) T waves were inverted, and the S-T segments were normal.

Vectorcardiograms were obtained in both patients and were consistent with left bundle branch block, showing conduction delay and abnormal initial forces directed leftward and posteriorly. In one patient, however, the loop rotated in a counterclockwise direction in the horizontal plane.

Group V. Control Group: The patients in this group with neither left ventricular hypertrophy

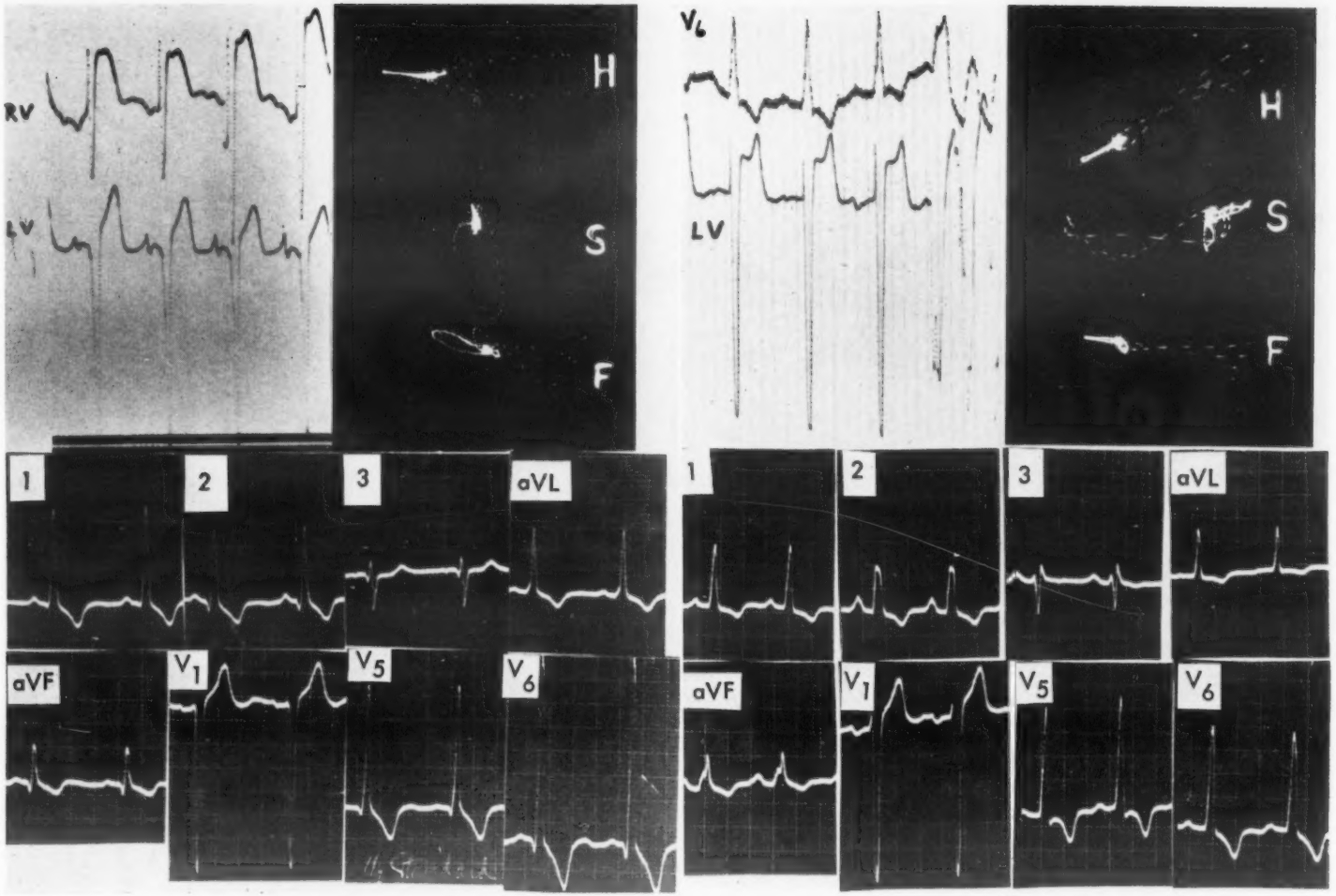

Fig. 3. (A) Case from group with left ventricular hypertrophy (lower leads). Endocardial leads (above left), showing right and left ventricular tracings. Vectorcardiogram above right. (B) Case 2 with incomplete left bundle branch block. Left ventricular endocardial tracing above left, recorded with V_6. Note the initial r deflection in the left ventricle and the ventricular premature beats. Time lines 0.1 sec. Paper speed 25 mm/sec. The vectorcardiogram (above right) and electrocardiogram (lower leads) are consistent with left ventricular hypertrophy.

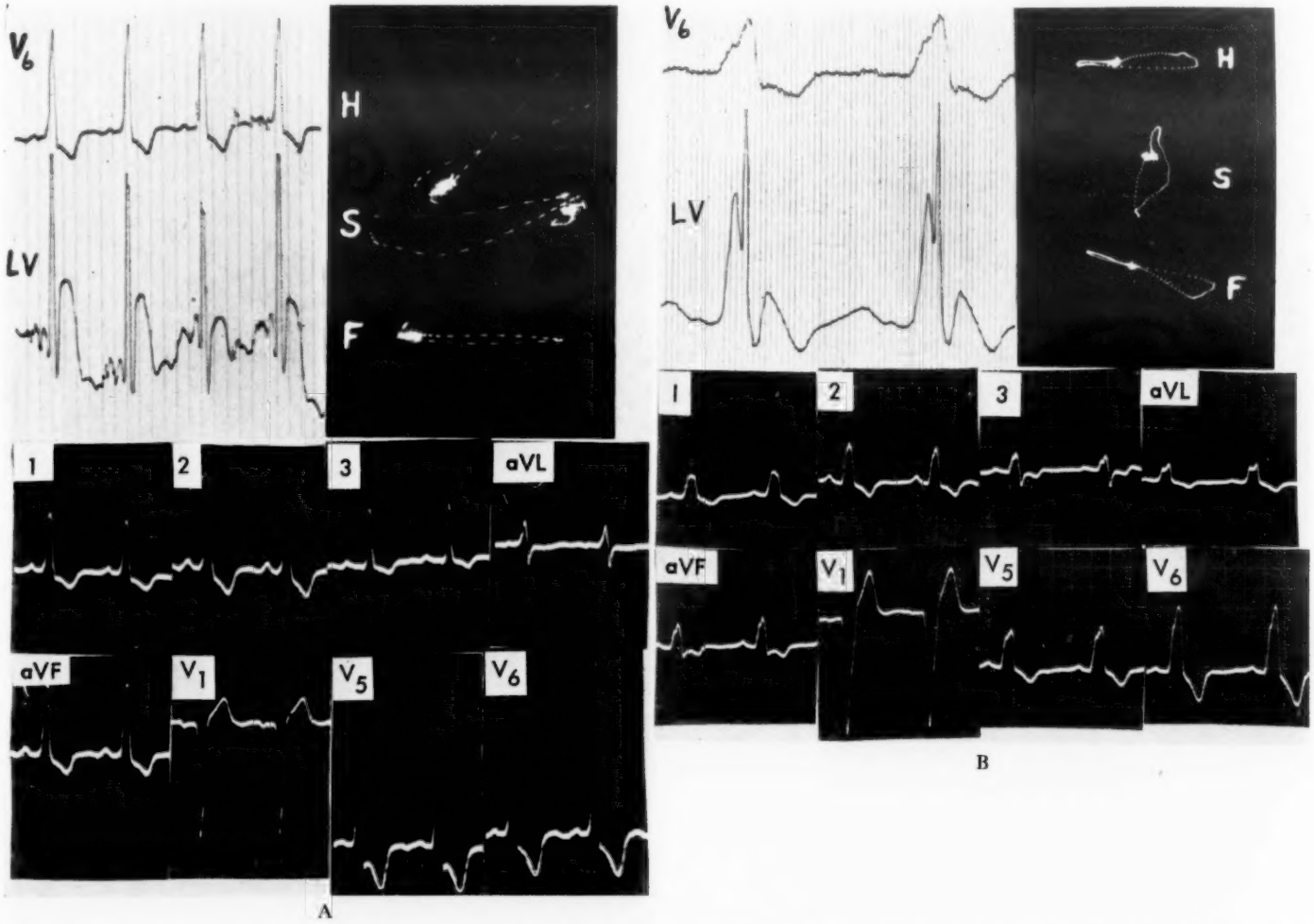

Fig. 4. (A) Case 7 with left ventricular hypertrophy and incomplete left bundle branch block. Left ventricular endocardial tracing (above left) recorded with V_6. Note the qRs complex in the left ventricle. Time lines 0.1 sec. Paper speed 75 mm/sec. The initial forces are directed posteriorly in the vectorcardiogram. Note slurring in leads 1, 2, aVF, V_5, and V_6 in the electrocardiogram. (B) Case 6 with complete left bundle branch block. Note the large RR′ left ventricular complex, recorded with V_6 (above left). Time lines 0.02 sec. Paper speed 75 mm/sec. Marked conduction delay is noted in the vectorcardiogram.

nor left bundle branch block were included for comparison only. In only one patient was a qRs recorded in the left ventricle (Table I, case 8). In all of the others a QS was observed. Right ventricular leads, obtained in 5 patients, recorded an rS pattern. An rsR′ and rsR′S′ pattern were seen over the pulmonic valve and in the right ventricular outflow tract in all (Fig. 5). As was reported in previous studies[11,12] and noted here, this type of complex in the right ventricle is not seen in severe left ventricular hypertrophy but is recorded in normals, and in patients with right bundle branch block or right ventricular hypertrophy.

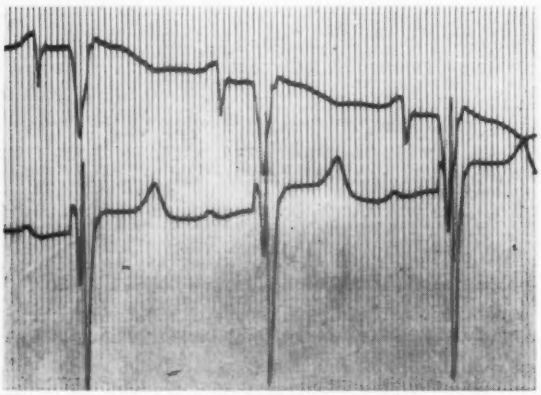

Fig. 5. Case from control group. Left ventricular tracing, above (sensitivity 9 mm/1 mv). Right ventricular tracings, below (sensitivity 6 mm/1 mv) showing an rsr′S′ complex recorded in the outflow tract in the patients of Group V. Time lines 0.02 sec. Paper speed 75 mm/sec.

Discussion

Although the specific mechanism of activation of the heart in left bundle branch block is still controversial, that is, whether abnormal conduction occurs in the interventricular septum and/or left ventricular free wall,[13–16] it is agreed that depolarization of the septum occurs from the contralateral to the blocked side. This concept originally presented by Lewis[17] and Wilson and associates[8] has been investigated and supported most recently by the use of unipolar and bipolar transeptal leads in dogs,[14] and by retrograde aortic catheterization of the left ventricle in man.[7,18] Thus, the demonstration of an initial positive deflection in the left ventricular cavity and an initial negative deflection in the right ventricle by endocardial leads indicates that septal activation in that area is proceeding abnormally from right to left.

Endocardial Lead in Left BBB: In complete left bundle branch block, which implies extensive involvement of the left bundle and an effective septal force directed from right to left, the recording of an initial positive deflection throughout the left ventricle would be expected. Thus, in our material an RR′ deflection of considerable duration and magnitude was recorded in a patient with complete left bundle branch block (Fig. 4B). In incomplete left bundle branch block, however, a variety of patterns (rS, qRs, qR, qrS, QS) has been observed both experimentally[19] and clinically as seen in this study, probably reflecting different degrees of block. It has been shown by Rodriguez and Sodi-Pallares in dogs[14] that in incomplete or intermediate degrees of block the activation wave, although delayed, may proceed in a normal direction in some regions of the left septal mass. More than one type of complex, including the normal QS pattern, may therefore be recorded in different areas of the left ventricular cavity in these cases, as was observed in some of our patients. In these patients both rS and QS complexes were also demonstrated in the right ventricle. Thus, the recorded deflection in the endocardial lead may be influenced by the degree and site of injury to the left bundle branch and by the over-all magnitude of the vector force developed from right to left.

Therefore, it can be seen that the limitation in exploration of the left ventricular cavity without a radiopaque catheter may explain the failure to demonstrate the initial r deflection in two of our patients with suggested evidence for incomplete left bundle branch block on the electrocardiogram. On the other hand, slurring of the R wave in leads facing the left ventricle in these cases may be due to so-called "arborization block"[19,20] within the left ventricular free wall. In the presence of an initial positive deflection, however, left bundle branch block, complete or incomplete, can be definitely entertained. This is likewise the case where purely negative complexes (QS) are recorded in all right ventricular positions. A left ventricular qR or qRs complex has also been

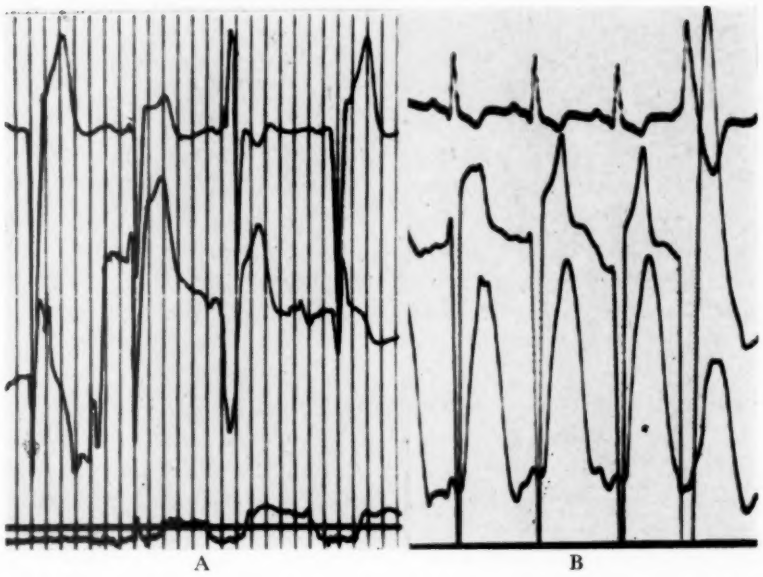

Fig. 6. The effect of right ventricular premature beats. (A) Note the left bundle branch block pattern with an initial R deflection produced in the left ventricular tracing (3rd beat, above), by the right ventricular endocardial lead (middle). The right ventricular pressure is recorded below. An rsR′ pattern is recorded in the right ventricle of this patient with right bundle branch block. (B) Note the change in the V_6 complex (above), particularly the slurring of the upstroke of R, resulting from the right ventricular premature beat (middle) produced by the right heart catheter. The right ventricular pressure is recorded simultaneously below.

identified with left bundle branch block through the experimental work of Sodi-Pallares and associates.[13]

Differentiation of Incomplete Left BBB and LVH: The presence of incomplete left bundle branch block as opposed to left ventricular hypertrophy alone proved to be difficult to establish from the standard electrocardiogram. It is of interest that in the group diagnosed as incomplete left bundle branch block by the endocardial lead, a similar diagnosis was made from the standard electrocardiogram in only one-half of the patients including one with complete left bundle branch block. Left ventricular hypertrophy alone was diagnosed in 4 patients, while atrial fibrillation and T wave abnormality due to digitalis were the only findings in another. No aid was derived from the activation time and QRS duration, and it is known that these measurements may be prolonged in both situations.[3,4,6,7]

In fact, as shown in this study and as previously reported, incomplete left bundle branch block may exist in the presence of a normal QRS duration. Somewhat more helpful was the simultaneous absence of r-V_1 and q-V_6. Thus, in one patient in whom the electrocardiogram had been interpreted as left ventricular hypertrophy alone, the simultaneous absence of r-V_1 and q-V_6 should have suggested left bundle branch block, as the left endocardial lead subsequently indicated. In comparison, although q-V_6 was variable, r-V_1 was present in all patients diagnosed as left ventricular hypertrophy alone by both the electrocardiogram and the endocardial lead. Both deflections, however, were present in some patients with incomplete left bundle branch block. This is not to be expected where abnormal depolarization of the septum from right to left occurs. It has been suggested by some investigators[7] that q-V_6 may be attributed to orientation of this lead to the left atrium. However, one of our cases with a q-V_6 demonstrated only an rS complex in the left atrium. As discussed above, more than one type of complex was obtained in many patients, some displaying an initial positive and some an initial negative deflection, indicating that some regions of the septum may be activated abnormally and others normally. If, in incomplete block, the latter predominates and

the over-all vectorial force is directed from left to right, an r-V_1 and q-V_6 may occur.

Significance of Slurring of QRS: Slurring of the ascending limb of R in leads facing the left ventricle proved to be most helpful in making the diagnosis of incomplete left bundle branch block. Discrepancies, however, were noted. In 4 patients without slurring, left bundle branch block was nevertheless demonstrated by the endocardial lead. The importance of slurring has been stressed by Sodi-Pallares and associates.[7] This was nicely illustrated in some of our patients in whom the production of right ventricular premature beats, producing transient or functional left bundle branch block,[21] caused striking changes in lead V_6 (Fig. 6).

The analysis indicates that although suggested electrocardiographic criteria for the diagnosis of incomplete left bundle branch block may be helpful in some cases, they may be inadequate in others, in which a diagnosis can be made only by a left ventricular endocardial lead.

The Vectorcardiogram in Left BBB: The diagnosis of left bundle branch block by the vectorcardiogram is likewise equivocal in many instances. The criteria suggested are still subject to disagreement. The leftward and posterior position of the vector loop may be similar in left bundle branch block and in left ventricular hypertrophy alone. The direction of inscription of the loop is apparently not characteristic.[10,22] Delay in inscription of the loop has not been noted in milder degrees of block[23] (Fig. 4A). Absence of anteriorly directed initial forces has also been inconsistently described[10,22,24] and may result in a pattern difficult to distinguish from anteroseptal infarction. Few vectorcardiograms were performed during this study. However, the findings are of interest in that they were characteristic only in the patients with complete left bundle branch block. In two patients with incomplete left bundle branch block in whom a vectorcardiographic diagnosis of left ventricular hypertrophy alone could be made, figure-of-eight loops were recorded in the horizontal plane without any other characteristics of block (Fig. 3B). In another patient in this group the criteria for left bundle branch block were met except for counterclockwise direction of the loop in the horizontal plane. Thus, the vectorcardiogram in these patients with incomplete left bundle branch block was suggestive in one patient only.

In conclusion, although technical difficulties at present preclude adequate exploration in every case, the demonstration of an initial positive deflection in the left ventricle by the endocardial lead indicates the presence of left bundle branch block most conclusively of the methods studied.

The electrocardiogram may often be difficult to interpret and the present criteria suggesting incomplete left bundle branch block are frequently questionable. It was found, however, that the simultaneous absence of r-V_1 and q-V_6 and the presence of slurring in leads facing the left ventricle proved most helpful in this respect. The vectorcardiogram on the other hand was the least reliable in clearly differentiating left ventricular hypertrophy from left bundle branch block.

Summary

(1) Thirty-one patients were studied by left endocardial and precordial leads, 14 with left ventricular hypertrophy, 5 with left ventricular hypertrophy and incomplete left bundle branch block, 2 with equivocal findings, 2 with complete left bundle branch block, and 8 with other diagnoses.

(2) The differentiation between left bundle branch block and left ventricular hypertrophy by the electrocardiogram and vectorcardiogram proved to be unsatisfactory in many cases.

(3) The endocardial lead appeared to be most useful in establishing the diagnosis of left bundle branch block when an initial positive deflection was demonstrated in the left ventricle.

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Electrical and Mechanical Asynchronism in the Cardiac Cycle

A Study of 100 Ventricular Premature Beats by Simultaneous Right and Left Ventricular Catheterization*

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ELECTRICAL ventricular asynchronism occurs in bundle branch block, complete heart block with idioventricular rhythm, the Wolff-Parkinson-White syndrome, and in ventricular premature beats or ventricular tachycardia. Theoretically, mechanical ventricular asynchronism would be expected under such circumstances—asynchronism in either the onset of ventricular contraction (onset of the isometric period of ventricular systole in the normal) or the onset of ventricular ejection (opening of the semilunar valve).

Earlier studies[1–23] have failed to demonstrate conclusively the presence or absence of mechanical ventricular asynchronism in the presence of electrical asynchronism. The development of right and left heart catheterization[24–31] has permitted simultaneous recording of right and left ventricular curves in man during ventricular premature beats, thereby affording an opportunity to determine whether mechanical asynchronism is a necessary consequence of electrical asynchronism.

MATERIAL AND METHODS

Right heart catheterization was performed in the usual manner, supine, in the basal postabsorptive state. Left heart catheterization was performed by a modification[31] of the posterior percutaneous transthoracic puncture technic of Fisher.[24] Two 7-in. long #17T needles were inserted into the left atrium. A polyethylene catheter was advanced through one needle into the left atrium and into the left ventricle. Left ventricular curves were recorded with Statham P23D or P23G strain gauges. Right ventricular curves were recorded on the proximal lumen of a Cournand double-lumen catheter, or on the middle lumen of a Cournand triple-lumen catheter, on Statham P23AA strain gauges.

Appropriate corrections for delay in pulse wave transmission in these catheter systems were made as described by Gordon *et al.*[40] This delay, to the nearest 0.01 sec, measured 0.01 sec for right ventricular curves, and 0.00 or 0.01 sec for left ventricular curves, according to the exact recording system employed.† All pressure curves

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† Employing the method of Gordon and Braunwald *et al.*[40] the delay in pulse wave transmission for a system composed of a right heart nylon catheter, (125 cm in length), black polyvinyl tubing 30 cm long, and a Statham P23AA strain gauge was noted to be 0.012 sec. The delay for a system composed of 22 in. of polyethylene tubing (passing through a 17T needle but not an 18T needle), 48 in. of black polyvinyl tubing and a Statham P23D strain gauge measured 0.006 sec. The delay for a

TABLE I

Physical Characteristics and Diagnoses in 18 Patients

Case No.	Cathet. #	Age	Sex	Diagnosis	Comments
1	61	34	M	Rh. HD EH MS AF Graham Steelle murmur, mild CHF III D	Recurrent mitral stenosis; mitral commissurotomy in 1950
2	75	49	F	Rh. HD EH MS MI AI AF III C	L.V.H. on fluoroscopy and ECG
3	119	36	M	Rh. HD EH AI AS NSR II C	Predominant AI
4	81	58	M	Rh. HD EH AS minimal AI AF angina pectoris III C	Mild non-obstructive pulmonary emphysema also present
5	70 91	33	F	Rh. HD EH MS AF II C	Previous arterial emboli; also studied 9 weeks after commissurotomy
6	85	28	M	Rh. HD EH MI MS AI AF III D	Giant left atrium
7	44	38	F	Rh. HD EH MS SB II C	L.A.-L.V. mean diastolic gradient less than 5 mm Hg at rest
8	69	30	F	Rh. HD EH MS NSR I B	1 month post-commissurotomy; III C pre-op
9	53	22	M	Rh. HD EH AI NSR I B	Palpitations represent only symptom
10	66	32	M	Rh. HD EH AS AI MS NSR I B	Asymptomatic
11	86	37	F	Rh. HD EH MS NSR I B	1 year post-commissurotomy; II C pre-op
12	110	42	M	Rh. HD EH MS NSR Graham Steelle murmur III D	Diastolic apical rumble not heard
13	104	40	M	Rh. HD EH MS NSR I B	10 months post-commissurotomy; III C pre-op
14	103	16	M	Cong. HD EH AS minimal AI NSR angina pectoris	Large mean systolic LV-BA gradient
15	99	46	F	Rh. HD EH AS AI MS NSR III C	Right bundle branch block present
16	98	42	F	Rh. HD EH MS MI NSR II C	1 year after mitral commissurotomy
17	95	53	F	Rh. HD EH MS minimal AS AF II C	Arterial emboli; minimal LV-BA systolic gradient
18	115	48	F	Rh. HD EH MS AF mild CHF III D	Graham Steelle murmur or minimal aortic insufficiency. Left ventricle not enlarged.

Rh.HD = Rheumatic heart disease; EH = Enlarged heart; MS = Mitral stenosis; AF = Atrial fibrillation; CHF = Congestive heart failure; MI = Mitral insufficiency; AI = Aortic insufficiency; AS = Aortic stenosis; NSR = Normal sinus rhythm; SB = Sinus bradycardia; Cong. HD = Congenital heart disease.

were recorded on a 6 channel cathode ray photographic recorder,‡ at a paper speed of 75 mm/sec; time lines were at 0.10, 0.04 or 0.02 sec intervals. Errors of parallax were thus eliminated.

One or more electrocardiographic leads were recorded simultaneously with the ventricular pressure curves, generally leads 1 and V_6, occasionally lead 1 or lead 3 (see Table II). Nineteen studies were made in 18 patients with rheumatic or congenital heart disease (Table I). When V_5 or V_6 was recorded, a predominantly upright premature QRS complex was interpreted as a right ventricular premature beat; a predominantly downward QRS complex was interpreted as a left ventricular premature beat. When lead 1 or lead 3 was recorded, an upright premature complex in lead 1 or a downward premature complex in lead 3 was interpreted as a right ventricular premature beat; a downward QRS complex

system made up of 36–48 in. of polyethylene tubing and a Statham P23D strain gauge equaled 0.004 sec. Finally, the delay for 36–48 in. of polyethylene tubing and a Statham P23G strain gauge measured 0.002 sec. The first system was used for recording all right heart pressures. The second system described above was used through catheterization #69 (Table I). The third system was employed through catheterization #111. The P23G strain gauge system was utilized for all catheterizations starting with #112 (Table I). The last three systems were employed for left heart catheterization.

‡ Electronics for Medicine, White Plains, N. Y.

in lead 1 or an upright complex in lead 3 was interpreted as a left ventricular premature beat.

Justification for this interpretation of the site of origin of ventricular premature beats from the precordial or limb leads may be found in the publications of Sodi-Pallares,[32] Barker,[33] and Holzmann.[34] Barker[33] states: "Left ventricular extrasystoles have the general appearance of right bundle branch block. Right ventricular extrasystoles bear a close resemblance to left bundle branch block." Barker *et al.*[35] produced ventricular extrasystoles in the exposed human heart in the course of pericardiostomy and noted that right ventricular beats produced upright deflections in lead 1; downward deflections were produced in extrasystoles from the left ventricle. These findings were confirmed by other investigators.[36,37] Wilson *et al.*[38] state: "There can be no reasonable doubt that, in man as in the dog, the potential variations of the right side of the precordium (leads V_1 and V_2) ordinarily resemble the potential variations of the anterior surface of the right ventricle, while the potential variations of the left side of the precordium (leads V_5 and V_6) ordinarily resemble the potential variations of the anterolateral surface of the left ventricle." Over 400 ventricular premature beats were produced in the exposed dog heart by Samet, Bernstein and Litwak.[39] Right ventricular stimulation resulted in an upright deflection in V_5; left ventricular stimulation resulted in a downward deflection in V_5.

Several hundred ventricular premature beats were recorded in man during right and left heart catheterization. Of these 100 were selected for study. The remainder were discarded because either the left or the right ventricular curve was considered technically inadequate for detailed time measurements, generally because of the degree of prematurity of the ventricular beat. The accurate measurement of the onset of the right or left ventricular pressure curve was difficult or impossible when the extrasystole occurred early in the cardiac cycle.

Results

The electrical-mechanical relationships for the right and left ventricular pressure curves during the predominant rhythm—sinus rhythm or atrial fibrillation—are illustrated in Table II. These time intervals are for conducted QRS complexes; the corresponding relationships for right and left ventricular premature beats are listed in Tables III and IV, respectively.

The range for QRS to upstroke of left ventricular pressure curve interval is shown in the fourth column, from 0.02 to 0.09 sec, corrected for mechanical delay in transmission of the pressure wave. The mode electrical-mechanical intervals are also listed, the most common intervals ranging from 0.04–0.06 sec. The range for QRS to upstroke of right ventricular pressure

TABLE II

Electrical-Mechanical Time Relationships During the Predominant Rhythm

Case number	Basic rhythm	ECG lead	QRS-LV interval (sec)		QRS-RV interval (sec)		LV-RV relationship (sec)	
			Range	Mode	Range	Mode	Range	Mode
1	Atrial fibrillation	Lead 3	0.03–0.06	0.05	0.04–0.06	0.05	0.00 to +0.01	0.00
2	Atrial fibrillation	Leads 1 and V_5	0.03–0.05	0.04	0.04–0.05	0.05	0.00 to +0.01	+0.01
3	NSR	Leads 1 and V_5	0.06–0.07	0.06	0.04–0.06	0.05	−0.02 to 0.00	−0.01
4	Atrial fibrillation	Leads 1 and V_6	0.04–0.07	0.04	0.03–0.06	0.04	−0.03 to +0.01	0.00
5	Atrial fibrillation	Leads 1 and V_6	0.04–0.07	0.05	0.06–0.08	0.07	+0.01 to +0.02	+0.02
	Atrial fibrillation	Leads 1 and V_6	0.05–0.07	0.06	0.04–0.07	0.04	−0.03 to +0.01	−0.01
6	Atrial fibrillation	Leads 1 and V_6	0.03–0.04	0.04	0.07–0.09	0.08	+0.03 to +0.05	+0.04
7	NSR	Lead 3	0.05–0.07	0.06	0.08–0.10	0.09	+0.02 to +0.03	+0.03
8	NSR	Leads 1 and V_6	0.03–0.04	0.03	0.03–0.05	0.04	0.01 to +0.02	+0.01
9	NSR	Lead 1	0.02–0.05	0.05	0.05–0.08	0.07	+0.02 to +0.03	+0.03
10	NSR	Leads 1 and V_6	0.04–0.07	0.06	0.04–0.07	0.06	0.00 to +0.01	0.00
11	NSR	Lead V_6	0.05–0.07	0.06	0.05–0.07	0.06	−0.01 to 0.00	0.00
12	NSR	Leads 1 and V_6	0.03–0.05	0.04	0.03–0.07	0.05	−0.01 to +0.03	+0.02
13	NSR	Leads 1 and V_6	0.06–0.08	0.06	0.06–0.09	0.08	0.00 to +0.02	+0.02
14	NSR	Leads 1 and V_6	0.06–0.07	0.07	0.09–0.11	0.10	+0.02 to +0.04	+0.03
15	NSR, RBBB	Leads 1 and V_6	0.04–0.07	0.05	0.07–0.10	0.08	+0.03 to +0.04	+0.03
16	NSR	Leads 1 and V_6	0.08–0.09	0.08	0.07–0.09	0.08	−0.01 to +0.01	0.00
17	Atrial fibrillation	Leads 1 and V_6	0.06–0.08	0.06	0.05–0.06	0.05	−0.03 to −0.01	−0.01
18	Atrial fibrillation	Leads 1 and V_6	0.06–0.08	0.06	0.05–0.07	0.05	−0.01 to +0.01	−0.01

TABLE III

Electrical-Mechanical Time Relationships During Right Ventricular Premature Beats

Case number	QRS-LV interval (sec)	QRS-RV interval (sec)	LV-RV relationship (sec)	Electrical-mechanical correlation	Electrical-mechanical delay
1	0.09	0.06	−0.03	No	None
	0.09	0.07	−0.02	No	None
	0.07	0.05	−0.02	No	None
3	0.12	0.13	+0.01	No	Both ventricles
7	0.15	0.07	−0.08	Yes	Left ventricle
8	0.12	0.07	−0.05	Yes	Left ventricle
	0.07	0.03	−0.04	Yes	None
9	0.12	0.15	0.03	No	Both ventricles
11	0.07	0.06	−0.01	No	None
	0.07	0.07	0.00	No	None
	0.08	0.08	0.00	No	None
	0.08	0.08	0.00	No	None
	0.08	0.07	−0.01	No	None
	0.11	0.10	−0.01	No	None
	0.10	0.07	−0.03	No	None
	0.08	0.07	−0.01	No	None
	0.07	0.07	0.00	No	None
	0.08	0.08	0.00	No	None
	0.08	0.08	0.00	No	None
	0.08	0.08	0.00	No	None
	0.08	0.08	0.00	No	None
14	0.10	0.09	−0.01	No	None
	0.12	0.11	−0.01	No	Left ventricle
15	0.12	0.06	−0.06	Yes	Left ventricle

curve interval is given in the fifth column, from 0.03 to 0.11 sec. The most common mode intervals are 0.05–0.08 sec.

The right ventricular-left ventricular upstroke relationships are shown in the sixth column. The range of these values is −0.03 sec to +0.05 sec. That is, the right ventricular upstroke preceded the left by 0.03 sec at one extreme; the left ventricular upstroke preceded that of the right by 0.05 sec at the other extreme. The normal range, therefore, somewhat arbitrarily has been defined as −0.03 to +0.03 sec. Any left-right ventricular upstroke relationship within this interval is defined as falling within the normal range. In a similar fashion any QRS to ventricular upstroke interval greater than 0.11 sec has been defined as showing electrical-mechanical delay in onset of ventricular isometric contraction.

Right Ventricular Premature Beats: Twenty-four right ventricular premature beats are analyzed in Table III. In 20 of the 24 premature beats, electrical asynchronism is not accompanied by mechanical asynchronism in onset of ventricular contraction. In 20 of the 24 beats, the time relationships between onset of right and left ventricular contraction falls between −0.03 sec and +0.03 sec. In 18 of the 24 complexes, the QRS to onset of ventricular contraction interval is normal, that is, less than 0.12 sec. In 4 beats the left ventricle alone is delayed; in 2 beats both ventricles are delayed.

TABLE IV

Electrical-Mechanical Time Relationships During Left Ventricular Premature Beats

Case number	QRS-LV interval (sec)	QRS-RV interval (sec)	LV-RV relationship (sec)	Electrical-mechanical correlation	Electrical-mechanical delay
1	0.07	0.10	+0.03	No	None
	0.12	0.11	−0.01	No	Left ventricle
	0.07	0.05	−0.02	No	None
	0.08	0.05	−0.03	No	None
	0.09	0.10	+0.01	No	None
2	0.08	0.13	+0.05	Yes	Right ventricle
4	0.08	0.09	+0.01	No	None
	0.11	0.14	+0.04	Yes	Right ventricle
	0.11	0.11	0.00	No	None
	0.12	0.09	−0.03	No	Left ventricle
5 (1)	0.12	0.15	+0.03	No	Both ventricles
	0.12	0.16	+0.04	Yes	Both ventricles
	0.12	0.15	+0.03	No	Both ventricles
	0.11	0.14	+0.03	No	Right ventricle
	0.12	0.15	+0.03	No	Both ventricles
	0.13	0.17	+0.04	Yes	Both ventricles
	0.13	0.16	+0.03	No	Both ventricles
5 (2)	0.14	0.18	+0.04	Yes	Both ventricles
	0.10	0.14	+0.04	Yes	Right ventricle
	0.08	0.05	−0.03	No	None
	0.08	0.05	−0.03	No	None
6	0.14	0.16	+0.02	No	Both ventricles
	0.12	0.16	+0.04	Yes	Both ventricles
	0.12	0.15	+0.03	No	Both ventricles
	0.13	0.16	+0.03	No	Both ventricles
	0.14	0.15	+0.01	No	Both ventricles
	0.12	0.12	0.00	No	Both ventricles
	0.10	0.15	+0.05	Yes	Right ventricle
	0.14	0.17	+0.03	Yes	Both ventricles
	0.13	0.17	+0.04	Yes	Both ventricles
	0.16	0.12	−0.04	Reverse	Both ventricles
	0.16	0.16	0.00	No	Both ventricles
	0.13	0.16	+0.03	No	Both ventricles
	0.13	0.16	+0.03	No	Both ventricles
	0.13	0.17	+0.04	Yes	Both ventricles
	0.15	0.16	+0.01	No	Both ventricles
	0.15	0.17	+0.02	No	Both ventricles
8	0.04	0.08	+0.04	Yes	None
	0.05	0.10	+0.05	Yes	None
	0.13	0.11	−0.02	No	Left ventricle
9	0.06	0.09	+0.03	No	None
	0.09	0.09	0.00	No	None
	0.10	0.12	+0.02	No	Right ventricle
10	0.13	0.13	0.00	No	Both ventricles
	0.10	0.13	+0.03	No	Right ventricle
	0.07	0.09	+0.02	No	None
	0.09	0.10	+0.01	No	None
	0.09	0.12	+0.03	No	Right ventricle
12	0.07	0.16	+0.09	Yes	Right ventricle
	0.06	0.11	+0.05	Yes	None
	0.06	0.05	−0.01	No	None
	0.08	0.16	+0.08	Yes	Right ventricle
	0.05	0.13	+0.08	Yes	Right ventricle
	0.06	0.11	+0.05	Yes	None
	0.06	0.10	+0.04	Yes	None
	0.09	0.14	+0.05	Yes	Right ventricle
	0.10	0.18	+0.08	Yes	Right ventricle
	0.08	0.13	+0.05	Yes	Right ventricle
13	0.09	0.10	+0.01	No	None
15	0.11	0.08	−0.03	No	None
16	0.11	0.13	+0.03	No	Right ventricle
	0.08	0.10	+0.02	No	None
	0.10	0.12	+0.02	No	None
	0.13	0.14	+0.01	No	Both ventricles
17	0.13	0.13	0.00	No	Both ventricles
	0.13	0.13	0.00	No	Both ventricles
	0.11	0.12	+0.01	No	Right ventricle
	0.07	0.13	+0.06	Yes	Right ventricle
	0.10	0.13	+0.03	No	Right ventricle
	0.14	0.13	−0.01	No	Both ventricles
18	0.14	0.15	+0.01	No	Both ventricles
	0.15	0.16	+0.01	No	Both ventricles
	0.12	0.13	+0.01	No	Both ventricles
	0.13	0.14	+0.01	No	Both ventricles
	0.10	0.13	+0.03	No	Right ventricle
	0.14	0.15	+0.01	No	Both ventricles

Left Ventricular Premature Beats: Seventy-six ventricular premature beats are analyzed in Table IV. In 52 beats mechanical asynchronism is not present, the relationship between onset of right and left ventricular pressure curves falling between −0.03 and +0.03 sec. In 23 complexes mechanical asynchronism is present. In 1 beat, the right ventricular upstroke precedes that of the left ventricle by 0.04 sec, despite origin of the premature beat in the left ventricle. In 22 complexes, the onset of ventricular contraction was within normal limits (QRS to ventricular onset <0.12 sec) for both ventricles. In 32 complexes the onset of ventricular contraction was delayed on both sides despite origin of the premature beat in the left ventricle. In 19 complexes only right ventricular contraction was delayed. However, in three beats, despite origin of the premature complex on the left side, the left ventricular complex was delayed but the right ventricular complex was not so delayed.

Summary of Findings: In summary, mechanical asynchronism was absent in 72 of 100 ventricular premature beats with widened aberrant QRS complexes. In 27 complexes mechanical asynchronism of the expected type (with the ventricular pressure curve on the side of origin of the premature QRS complex preceding that of the opposite ventricle) was noted. In one instance, reverse mechanical asynchronism was found, the right ventricular upstroke preceding that of the left by 0.04 sec, despite origin of the premature beat in the left ventricle. It is of considerable interest that the QRS-ejection interval was delayed for both ventricles in 34 instances, despite the univentricular onset of the premature beat. In three instances only the ipsilateral ventricle was delayed in onset of contraction, a finding opposite to that to be expected.

Examples of these relationships are illustrated in Figures 1 to 4. In Figure 1, the left ventricular upstroke precedes the right by 0.03 sec in the first and third beats, the normally conducted sinus beats. The right ventricular beats are corrected by 0.01 sec. In the middle complex, a right ventricular premature beat, the ventricular upstrokes are identical in time; when corrected for pulse wave transmission delay, the right ventricle precedes the left by 0.01 sec. In Figure 2, the right ventricular upstroke precedes the left by 0.01 sec in the normally conducted first and last beats. The right ventricular curve is corrected by 0.01 sec. In the second complex, a left ventricular premature beat, the left ventric-

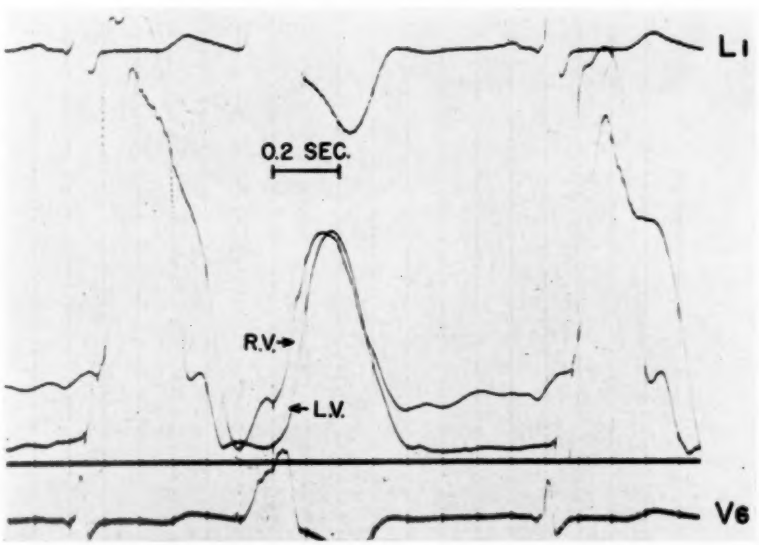

Fig. 1. In the normally conducted first and third beats, the onset of left ventricular contraction precedes that of the right ventricle by 0.03 sec. In the right ventricular premature beat (second beat), the right ventricular onset precedes that of the left by 0.01 sec when the former is corrected for pulse wave transmission delay. Note however that whereas the left ventricular upstroke precedes that of the right in the first and last beats, in the middle beat the reverse is true.

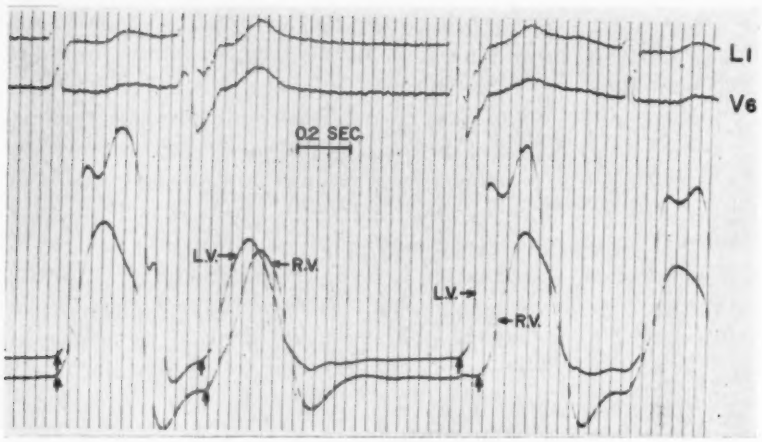

Fig. 2. Mechanical asynchronism is absent in the first ventricular premature beat (second complex) but is present in the second (third complex). See text.

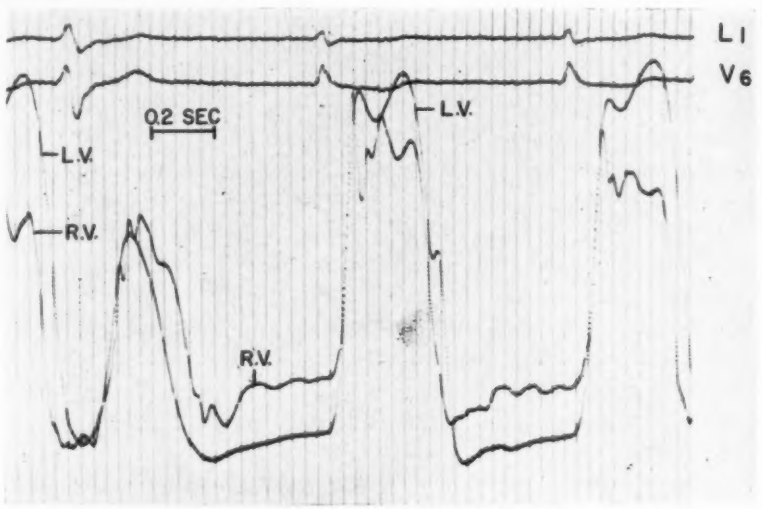

Fig. 3. Mechanical asynchronism is absent following the left ventricular premature beat (first complex). See text.

ular upstroke is 0.01 sec ahead of the right, when a suitable correction (0.01 sec) is applied to the QRS-right ventricular interval. However, the third complex demonstrates mechanical asynchronism, the left ventricular upstroke preceding the right by 0.06 sec. In Figure 3 the left and right ventricular upstrokes are identical in the normal beat, the second and third complexes. The right ventricular curve is corrected by 0.01 sec. In the first complex a left ventricular premature beat, the left ventricular upstroke is at the same time as that of the right, if 0.01 sec is subtracted from the QRS-right ventricular upstroke to correct for mechanical delay in pulse wave transmission.

Figure 4 illustrates one further point. In the normal first beat, the left ventricular upstroke precedes the right by 0.02 sec (0.03 sec on the tracings, before the right ventricular curve is corrected by 0.01 sec). The next 3 beats are left ventricular premature beats, and mechanical asynchronism is present in all three. However, the point to be emphasized is that in the first beat, the entire upstroke of the left ventricular curve is slightly ahead of that on the right side. In the left ventricular premature beats, the largest portion of the left ventricular upstroke is well ahead of that on the right. The same phenomenon is demonstrated in the middle beat of Figure 1 where the *onset* of right and left ventricular contraction is identical in time, yet the major portion of the right ventricular upstroke precedes that of the left, a reversal of the relationship noted in the two normal beats.

Discussion

Many studies have been reported relative to the problem of whether mechanical asynchro-

nism in onset of ventricular contraction is a necessary consequence of electrical asynchronism in depolarization as occurs in ventricular premature beats and complete bundle branch block. In the great majority of these reports only indirect evidence dealing with the basic problems was obtained. Eppinger and Rothberger[1,2] produced bundle branch block experimentally and then noted a delay in the pulse wave from that side. Wolferth and Margolies[6,7] studied 11 cases of left bundle branch block, measuring the interval from the onset of the QRS complex to the beginning of the right carotid artery pulsation in the neck. In normals this interval ranged from 0.09 to 0.15 sec, average 0.11 sec. In the subjects with bundle branch block, the range was 0.16 to 0.21 sec, average 0.17 sec. Wolferth and Margolies also employed various combinations of the electrocardiogram, heart sound tracings, apex cardiograms, venous pulse tracings, and roentgenkymographic tracings of aortic and pulmonary artery pulsations. From these studies the conclusion was reached that correlation between electrical and mechanical asynchronism had been demonstrated. Nichol[8] came to the same conclusion as a result of a similar study.

Castex and his associates[9] found that they could correlate the site of origin of ventricular premature beats with the interval from the onset of the QRS complex to the onset of the carotid artery pulse with fair success. In 10 cases, when the QRS complex of a ventricular premature beat was downward in lead 1 (therefore, a left ventricular premature beat), the QRS to carotid upstroke interval ranged from 0.11 to 0.22 sec, average 0.17 sec. In 13 cases, when the QRS complex of a ventricular premature beat was upright in lead 1 (therefore a right ventricular premature beat), the QRS to carotid upstroke interval ranged from 0.16 to 0.28 sec, average 0.22 sec. Kossman and Goldberg[10] and Richards, Cournand and co-workers,[11,12] Eppinger *et al.*[1,2] and Ellinger *et al.*[19] have also published data in man interpreted as demonstrating delayed mechanical activity on the ipsilateral side in subjects with bundle branch block. In none of these studies was a direct comparison of the relationship between onset of right and left ventricular pressure curves possible.

On the other hand, Katz[13] noted that the pulse wave was not delayed in the carotid artery in most patients with bundle branch block. Samet, Mednick and Schwedel[21–23] were able to demon-

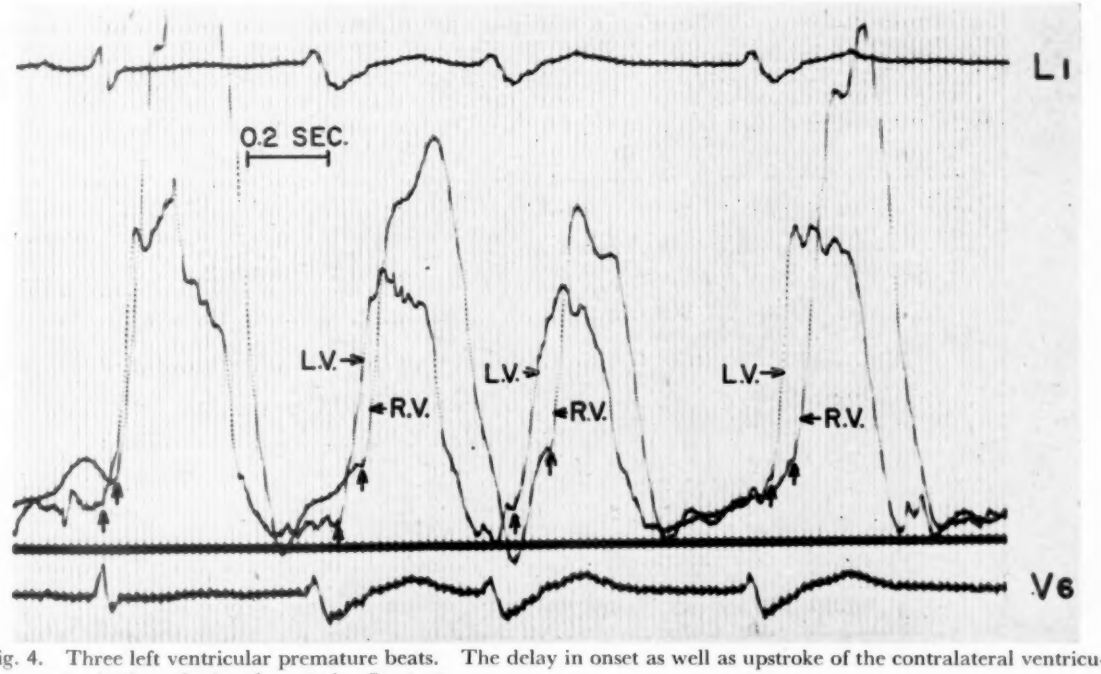

Fig. 4. Three left ventricular premature beats. The delay in onset as well as upstroke of the contralateral ventricular pressure in the pulse is to be noted. See text.

strate ventricular mechanical asynchronism in only one-third of 61 patients with complete bundle branch block studied by simultaneous electrokymography of the ascending aorta and pulmonary artery. Braunwald and Morrow[41] have confirmed these findings recently by simultaneous catheterization of the right and left ventricles in 15 patients with complete bundle branch block, 5 with left bundle branch block and 10 with complete right bundle branch block. Unfortunately, vectorcardiographic data were not available in the subjects with right bundle

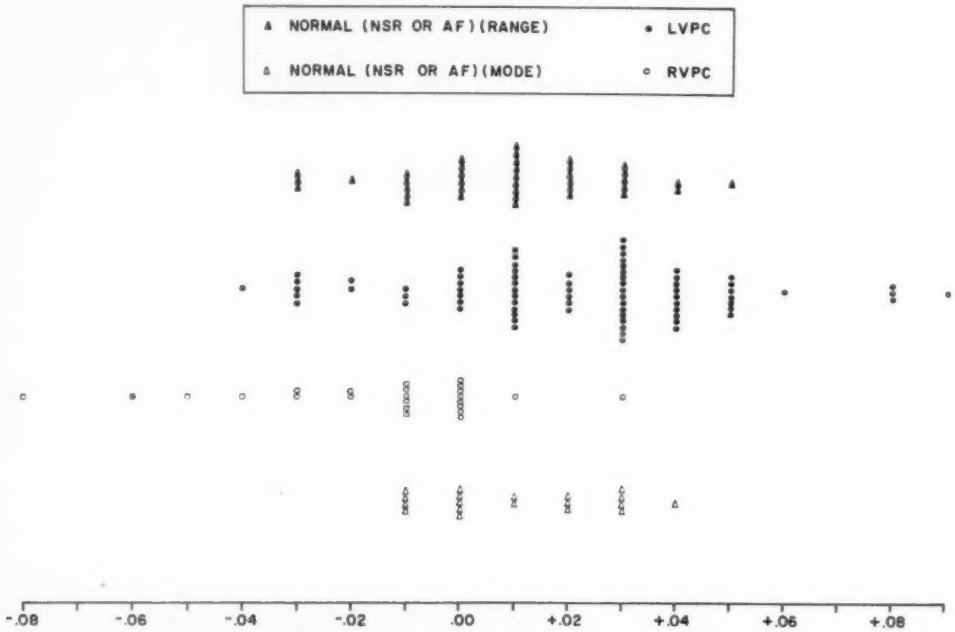

Fig. 5. Time relation between onset of right and left ventricular contraction. The normal range has been taken as −0.03 to +0.03 sec. That is, at one extreme the right ventricular upstroke precedes the left by 0.03 sec (−0.03); at the other extreme the left upstroke precedes the right by 0.03 sec (+0.03). The lowermost row is the mode figure for conducted beats in 19 studies in 18 patients. The upper row is the range data for conducted beats—hence there are twice as many points as in the lowermost row. The two intermediate rows are for the premature ventricular beats.

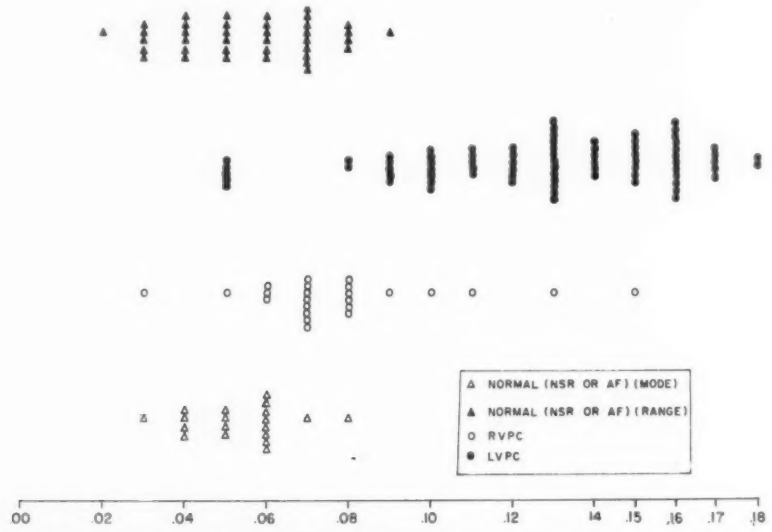

Fig. 6. Time relation between onset of the QRS complex and right ventricular contraction. "Normal" refers to conducted QRS complexes, either during atrial fibrillation or normal sinus rhythm.

branch block, so that right ventricular hypertrophy may have merely simulated right bundle branch block, as may occur in right ventricular hypertrophy due to interatrial septal defect or mitral stenosis. The postmortem studies of Yater,[42] which revealed bilateral lesions in the bundle branches in human bundle branch block regardless of the side of the bundle branch block, are consistent with these data from combined right and left heart catheterization.

Wiggers[16] notes: "When the intraventricular pressures are simultaneously recorded from the left and right sides of the heart, the reactions to artificial stimuli differ appreciably on the two sides. In the first place, the pressure within the ventricle stimulated begins to rise from 0.03 to 0.08 of a second earlier than in the other ventricle." These results could not be confirmed by Samet, Bernstein and Litwak.[39] The data in this present study deal with comparison of the onset of right and left ventricular contraction on the corresponding pressure curves obtained during simultaneous right and left heart catheterization. In most instances (72 of 100 beats) of right and left ventricular premature beats, asynchronism beyond the limits observed during conducted beats was not noted. These findings agree with those noted during earlier studies[21-23] employing simultaneous electrokymography of the ascending aorta and pulmonary artery. In this older study mechanical asynchronism could be demonstrated in only approximately one-third of the subjects.

Analysis of the Data: Graphic analysis of the results of the present study is of interest. In Figure 5 the mode time relation between *onset* of right and left ventricular contraction is given on the lowermost horizontal row of points; the corresponding figures for the range are shown on the uppermost row (Table II). It is readily seen that the onset of most of the right and left ventricular premature systoles fall in the normal range, i.e., between −0.03 to +0.03 sec. The time relation between onset of the QRS complex and onset of right ventricular contraction is illustrated in Figure 6. The data for the normally conducted QRS complexes are given in the lowermost row (mode) and uppermost row (range). The open circles are for the right ventricular beats; the closed circles are for the left ventricular beats. The QRS-right ventricular interval is normal or minimally delayed for the right ventricular premature beats. However, the QRS-right ventricular interval is ob-

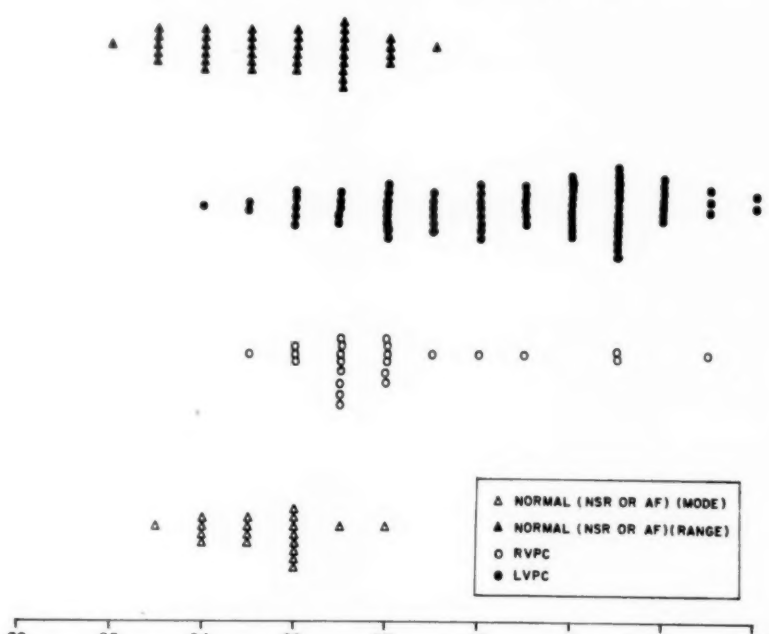

Fig. 7. Time relation between onset of the QRS complex and left ventricular contraction. "Normal" has the same meaning as in Figure 6.

viously delayed in most left ventricular premature systoles. This latter observation might lead to the conclusion that ventricular mechanical asynchronism is to be noted, since the onset of right ventricular contraction is delayed only with the left premature systoles, but not with the right premature beats. However, inspection of Figure 7 reveals that the QRS-left ventricular interval is also delayed during left ventricular beats, but not during right ventricular beats. In short, the QRS-ventricular onset is delayed for both ventricles during left ventricular premature beats. During right ventricular beats, the bilateral delay is minimal.

Causes for Lack of Mechanical Asynchronism: The question as to why such mechanical asynchronism is not found more frequently has been previously discussed in some detail.[43] With respect to ventricular premature beats, two observations are pertinent. First, each of the four discrete muscle bundles comprising the two ventricles (superficial sinospiral and bulbospiral, and deep sinospiral and bulbospiral muscles) contributes to the formation of each ventricle.[44] Gregg[45] has stated: "It is probable that both deep muscle bundles have a dominant function in emptying both ventricles." Rushmer[46] has expressed similar views. Under these conditions ventricular mechanical asynchronism is not to be expected even in the presence of electrical ventricular asynchronism, since it is difficult to conceive of one ventricle contracting without the other also doing so. Secondly, there are several observations in the literature which demonstrate that mechanical and electrical events in the cardiac cycle can be separated. Mines[47] showed that perfusion of a frog's heart with a calcium-free solution resulted in almost complete abolition of the mechanical beat while the simultaneously recorded electrocardiogram remained unchanged. Bertha[48] and Bertha and Schutz[49] have come to similar conclusions.

Findings in Bundle Branch Block: Our data on simultaneous right and left heart catheterization in patients with bundle branch block are limited to two patients to date. In one patient with complete left bundle branch block (with vectorcardiographic as well as electrocardiographic data verification), the onset of ventricular contraction was almost simultaneous in the two ventricles; in another with complete right bundle branch block (with vector confirmation) the left ventricular upstroke preceded that of the right by 0.03 sec. In view of these data as well as those of Braunwald and Morrow, and previously published electrokymographic data, it is of interest to note that recent textbooks in cardiology,[50,51] and recent papers,[52,53] continue to support the concept of mechanical ventricular asynchronism in patients with complete bundle branch block. The absence of ventricular asynchronism may be related to the fact that histologic studies[42] of the conduction system in complete bundle branch block have frequently shown lesions in both bundle branches.

Summary

Electrical ventricular asynchronism may occur in man in bundle branch block, complete heart block with an idioventricular rhythm, ventricular premature beats and the Wolff-Parkinson-White syndrome. This paper is a study of the problem of whether mechanical ventricular asynchronism is a necessary consequence of electrical ventricular asynchronism such as occurs in the above situations. The data were obtained in intact man during the course of simultaneous right and left heart catheterization. The results indicate that mechanical ventricular asynchronism is infrequently seen in ventricular premature beats produced during the course of simultaneous combined heart catheterization. Mechanical asynchronism in onset of ventricular isometric contraction was absent in 72 of 100 ventricular premature beats with widened aberrant QRS complexes.

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Intracardiac Electrocardiography

Observations During Left Heart Catheterization in Man*

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SINCE 1945, a number of reports have appeared on intracardiac electrocardiography of the right heart in man. By accident, during right catheterization in cases of congenital heart disease, the catheter would pass through a septal defect into one of the left chambers, and thus record left intracavity potentials. In this way, Sodi-Pallares[1, Fig. 8] described a QS pattern inside the left ventricle in a case of complete right bundle branch block. Duchosal[2, Fig. 4] recorded a left atrial pattern in a case with patent foramen ovale. Kert,[3, Fig. 3] in a similar way, obtained a unipolar lead from the cavity of the left atrium. Among recent publications, Latour and Puech report in their book[4] a number of tracings from the left cavities during right heart catheterization.

Only in 1950, a technique for arteriography of the thoracic aorta[5] was first used for retrograde catheterization of the left ventricle.[6–9] Three other papers on left intracardiac electrocardiography followed in 1951[10–12] and one in 1952.[13] Of very recent date is a report by Brusca *et al.*[14] of left intracavity potentials recorded on the operating table during mitral commissurotomy.

Unquestionably, in spite of the interest of these investigations, the limited number of papers and the small series of cases studied are explained by the serious dangers inherent in the technique, as commented on by Laubry in discussing Coelho's work.[11] Moreover, with retrograde catheterization, a systematic exploration of the left atrium could not be attempted.

The transthoracic approach of left heart catheterization has made available to us a new means of investigation of intracardiac electrocardiography.

Atrial Activation: As far as the left atrial potentials are concerned, the esophageal lead at atrial level has long been considered the only semidirect lead of the left atrium, and is still widely used in clinical electrocardiography. This stems from the classic work by Lewis and Rothschild[15] controlled by subsequent investigators,[16] who demonstrated the radial spread of the wave of depolarization in the atria as opposed to the endo-epicardial transmission of activation in the ventricles. As a consequence, the same atrial potentials can be recorded from the endocardial as well as the epicardial surfaces, and thus from the semidirect esophageal lead.

Recently, the potentials of the left atrium have been investigated by direct epicardial leads in the course of thoracic surgery, both in normal and in pathologic cases.[17,18] In addition, semidirect leads for the left atrium have been described from cardiac structures surrounding or close to the atrium. For instance, Kossmann[19] interpreted the potentials from the left pulmonary artery as being due to the left atrium; Coelho[11] described atrial potentials recorded from the first portion of the descending aorta as reflecting those of a dilated left atrium. For Levine *et al.*[20] the currents recorded in the coronary sinus and in the great cardiac veins represent the "accessible left atrial potentials." This point is best illustrated by Latour and Puech who present a figure[4, Fig. 7] in which a close resemblance is seen between the tracing taken in the lateral part of the left atrium and that recorded in the middle part of the great cardiac vein (patient with atrial septal defect). These various unipolar leads, on one hand, supply the proof of the radial spread of the atrial

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activation wave in man, but on the other hand, they reflect the attempts of investigators to record potentials of the left atrium in a routine manner during right heart catheterization.

Ventricular Activation: In the field of electrophysiology of the heart, important landmarks have been achieved through extensive anatomic and physiologic studies.[21]

With normal intraventricular conduction, the first part of the ventricular myocardium to be activated is in the middle third of the left septal surface, where the left branch of the bundle starts to fan out. This activation results in an early vector which, in the absence of abnormal rotation, is directed from left to right toward the trabecular zone of the right ventricle, at the base of the anterior papillary muscle. To the right of the septum, this vector is responsible for an *r wave*, both within the right ventricle and in leads overlying this chamber. To the left of the septum, this early vector is responsible for the first part of the negative deflection of the left ventricular cavity and the *q wave* of leads facing this chamber. As the first septal vector is directed toward the trabecular zone, the *r wave* within the right ventricle is greater near the apex than in higher parts of this chamber, where it may be normally absent. Following septal activation, the Purkinje network of the two ventricles becomes excited and the free ventricular walls are activated in a radial direction, so that, at this time, a negative deflection is inscribed in both ventricular cavities. Thus, the resulting ventricular complex as recorded by unipolar intracardiac leads is *rS* in the right ventricle and *QS* in the left.

Experimental work by Kennamer *et al.*,[22] confirmed by Durrer *et al.*[23] and by Sodi-Pallares and associates,[24] seems to indicate that the subendocardial two-thirds of the left ventricle does not participate in the formation of the potentials which are recorded over the precordium or epicardium. The reason for this is the almost instantaneous and multidirectional activation of these subendocardial portions; the vector of ventricular depolarization is then due to the activation wave spreading through the subepicardial outer third of the ventricular wall in an outward direction.

These studies of intracardiac electrocardiography have been correlated with extensive investigations by direct epicardial leads during thoracic surgery in man,[25] and it has been shown that the first parts to be activated are the right paraseptal areas, followed almost instantaneously by the apices of both ventricles, then by intermediate zones, and finally by the basal portions of the two ventricles.

Ventricular Complex Recorded in the Atria: Some controversy has arisen as to the ventricular complex recorded within the two atria by unipolar intracardiac leads. In the right atrium, the ventricular complex consists of a predominantly negative deflection with a "*late R*," due to the late activation of the basal portions of the right ventricle, for it increases both with right bundle branch block and right ventricular hypertrophy. This *late R* should be differentiated from an "*early r*," frequently recorded at low atrial levels, which is related to the early vector of septal activation. The existence of a similar *late R* pattern of the ventricular complex within the normal left atrium in man has been postulated because it is often found in esophageal leads at atrial levels and has been recorded accidentally in cases of atrial septal defect.[4] Moreover, a *late R* is commonly recorded in the left atrium of the dog and it increases after experimental production of left bundle branch block as a result of a late vector of depolarization of the posterobasal portions of the left ventricle.[26]

The normal process of repolarization is represented by negative, asymmetrical T waves in all cardiac chambers. Therefore, in normal subjects, there is a discordance between left intracardiac and left precordial T waves.[27]

Material

This study was based on intracardiac tracings of the left atrium and ventricle in 15 cases. One was a case of syphilitic aortic insufficiency, while the 14 others were cases of rheumatic heart disease with mitral or aortic valvular lesions, in whom left heart catheterization was undertaken in order to evaluate the severity of the lesions in view of possible corrective surgery.

Three additional cases were discarded because of failure of the catheter to pass through the mitral valve into the left ventricle. This was attributed to a marked regurgitant jet of mitral insufficiency. In eight of the cases, catheterization of the chambers of the right heart was also performed. Following evaluation of the catheterization data, the 14 rheumatic cases were separated in three groups: a first group of nine cases with predominant mitral stenosis and various degress of mitral insufficiency; a second group of two cases with moderate mitral stenosis, minimal insufficiency, and severe aortic stenosis; and a third group of three cases with pure mitral insufficiency. Four cases had atrial fibrillation; two cases had atrial flutter. Isolated right ventricular hypertrophy was present in five cases; in two more instances, there was an associated left ventricular hypertrophy. In one case the peripheral electrocardiogram was considered within normal limits. Four cases showed evidence of isolated left ventricular hypertrophy; and in three other cases, the pattern of left ventricular "strain" was present.

Technique

In our laboratory, left heart catheterization has been done since 1955, according to the method of Björk,[28] with the modifications of Kent *et al.*[29] and Fisher.[30] No major complications, like those mentioned by other investigators,[31,32] were ever encountered.

During the procedure, by far the most frequent arrhythmia was represented by *left ventricular premature beats*, which were elicited only through direct stimulation

of the ventricular endocardium by the tip of the catheter. By contrast, it was rare to see atrial arrhythmias with the needle in the left atrium or while maneuvering the catheter in the attempts to pass it into the ventricle. When repeated premature beats occurred, the catheter was changed in its position or completely withdrawn, so as to prevent more dangerous ventricular arrhythmias. It is our belief that a cautious and attentive technique is the most important factor in making left heart catheterization a safe procedure.

The recording of *intracardiac electrocardiograms*, as previously reported,[33] was based on the electric conduction by a column of sterile 5 per cent saline solution into the catheter and the use of Wilson's central terminal. The unipolar intracardiac leads obtained in this way were proposed to be called *intracardiac V-leads:* V-RA, V-RV, V-LA, V-LV, V-AO, and V-PA, respectively.

A standardization of 0.1–0.2 N was used for ventricular tracings; after pullback into the atrium, the amplification was usually increased to 0.5 N. At least three pullback maneuvers were obtained in every case. Three different film speeds were used: 25, 50, and 100 mm/sec.

Pressure tracings were recorded with a Statham P 23 D strain gauge. The recording apparatus was a 6 channel universal cardiograph with cathode-ray oscilloscopes, built by Electronics for Medicine.

Results

LEFT ATRIAL INTRACARDIAC TRACINGS

(*A*) *Atrial Complex:* The cases were divided into three groups, depending on the cardiac rhythm:

(1) Seven cases with normal sinus rhythm: the P wave fell in the 2nd part of the P wave in simultaneously recorded limb leads. The asynchronism of the intrinsicoid deflection of the intracardiac P wave varied between 0.05 and 0.09 sec in cases with predominant mitral stenosis.

(2) Six cases of atrial fibrillation: no evidence of coordinated electrical activity was recorded. However, in some cases, small, slightly irregular waves were recorded.

(3) Two cases of atrial flutter: "f" waves were recorded in both cases.

(*B*) *Ventricular Complex:* The QRS presented the same characteristics as the one recorded inside the left ventricle, though usually of lower voltage. In cases of left ventricular hypertrophy, high voltage was recorded with QS or QR patterns according to the atrial level. ST and T wave alterations, parallel to those recorded in the ventricle, were noted, except in one case.

LEFT VENTRICULAR INTRACARDIAC TRACINGS

(*A*) *Atrial Complex:* In cases with sinus rhythm, the P wave was positive and of very low voltage, due to the low amplification used. In one of three cases of pure mitral insufficiency, the P was tall and peaked. In cases of atrial fibrillation or flutter, no atrial activity was recorded.

(*B*) *Ventricular Complex:* The following variations were noted:

(1) In five cases of isolated right ventricular hypertrophy a normal intracardiac tracing was recorded. The T wave was always negative.

(2) Left ventricular premature beats presented a widened QS pattern and secondary ST and T changes.

(3) In cases of left ventricular hypertrophy or "strain" there was increased voltage of QRS.

(4) ST and T wave alterations seemed to vary according to the level of the catheter tip within the ventricle. Generally the changes were in an opposite direction to those of the left precordial leads.

(5) During a pullback maneuver, there was a progressive flattening of the T wave, whether negative or positive. However, the ventricular complex usually presented a sharp change from a ventricular to an atrial pattern, both in normal and pathologic cases.

Discussion

GENERAL CONSIDERATIONS

In the interpretation of intracardiac electrocardiograms, recorded by means of a catheter, special considerations should be kept in mind because these unipolar leads differ in many aspects from any other. The electrical potentials conducted through the catheter are a function of the solid angle formed by the tip of the catheter and the intracardiac structures. Thus, selective patterns can be derived from each chamber, and, for the same chamber, individual parts can be investigated.*

More recently, Johnston and Willis[34] recognized that, from a strictly morphologic viewpoint, the gap between experimental and clinical electrocardiography has been closed by this new

* This is possible in the case of the right heart, not in that of the left (soft catheter).

development of investigation. On the other hand, the same authors express a justified criticism as to the absolute values of the recorded voltages.

Theoretically, the solid angle formed by the tip of the catheter presents continuous variations

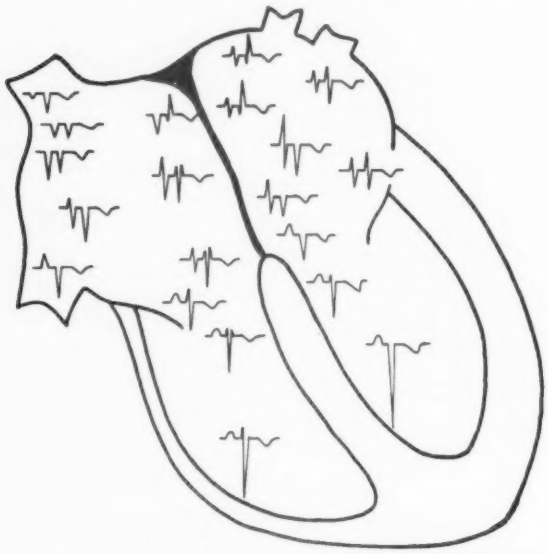


Fig. 1. Scheme of normal patterns of atrial and ventricular complexes recorded by a unipolar lead at various levels within the cardiac chambers. The *rS* pattern, found in high portions of the left ventricle, will be discussed in the text.

due to its shifting with the motions of the heart and the respiration. Even if the tip of the catheter can be easily located on fluoroscopy, its exact distance from the endocardium cannot be determined. From the inverse square law, the amplitude of a deflection is dependent upon the square of the distance between the exploring electrode and the source of electrical potentials. It follows that deflections of high voltage may simply mean that the electrode is very close to a portion of activated myocardium, and only in this instance can the intracardiac lead be considered as a direct lead. In order to overcome this drawback, the method of "slow pullback," suggested by Emslie-Smith,[35] has been used in our laboratory in view of the obligatory route that the catheter would follow within the same chamber and from one chamber to the next. With this method, the shifting of the catheter is greatly reduced so that the electrical potentials can be calculated. It should be further pointed out that the above considerations represent a criticism of the catheter technique itself. Even with these reservations, intracardiac electrocardiography assumes a unique value: hypothetical patterns, postulated for a long time, can now be actually recorded.

ELECTROCARDIOGRAM RECORDED WITHIN THE LEFT ATRIUM

The normal patterns of atrial and ventricular complexes at various levels within the cardiac chambers are presented schematically in Figure 1. For comparison, Figure 2 shows the epicardial potentials recorded by direct leads during thoracic surgery in patients with normal circulatory system, according to Barbato.[25] The terminology for intracardiac deflections is that proposed by Hecht[36] and generally accepted.

Left Atrial Pattern: The most frequent pattern inside the left atrium is that of a *diphasic P wave*, due to the right-to-left vector of atrial depolarization: this is followed by a *QS complex* and by a *negative T wave*, both reflecting ventricular processes. In higher portions of the atrium, a *Qr* or *QR* is consistently found: the late positive deflection seems to be an expression of the late

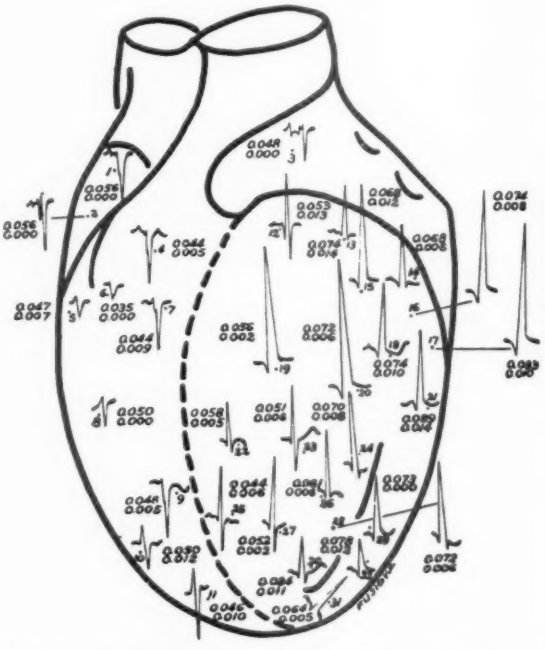


Fig. 2. Scheme of normal epicardial potentials recorded by direct epicardial leads during thoracic surgery, according to E. C. D. Barbato.[25]

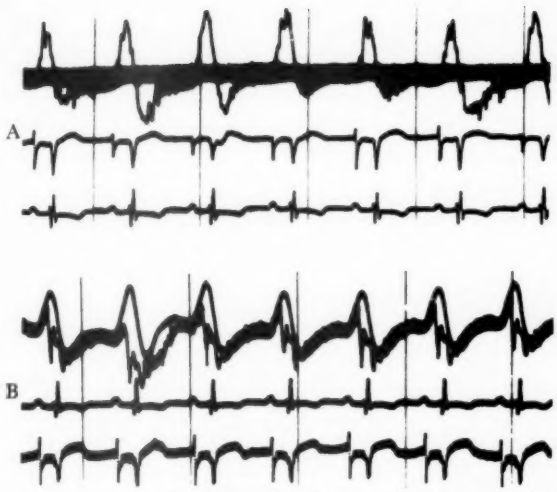


Fig. 3. Case of atrial septal defect. (A) Right atrial pressure curve, lead V-RA and simultaneous lead 2. (B) Left atrial pressure curve, lead 2, and V-LA. Film speed: 25 mm/sec. The normal asynchronism between right and left atrial activations is apparent. The P wave in lead V-RA falls in the first half of the P wave in the peripheral ECG; the P wave in lead V-LA falls in the second half. Calculated asynchronism: 0.035 sec.

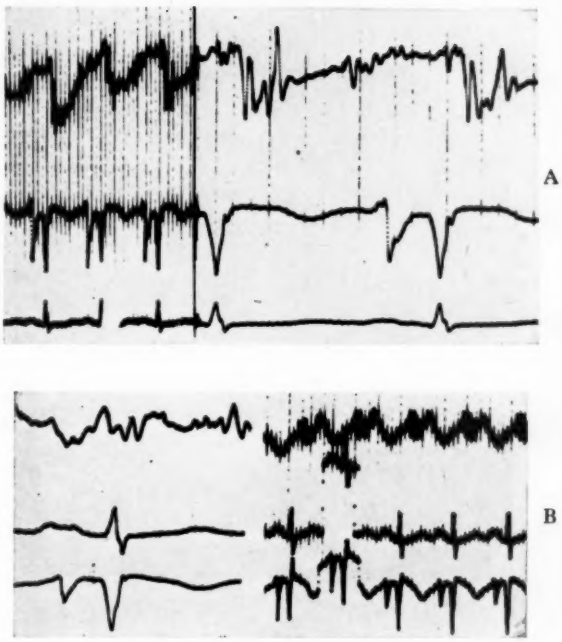


Fig. 4. Case of mitral stenosis. (A) Right atrial pressure curve, V-RA and lead 2. (B) Left atrial pressure curve, lead 2, and V-LA. Film speeds: 25 and 100 mm/sec. The asynchronism between the peripheral P wave and the P in V-LA is increased due to late inscription of the intrinsicoid deflection of V-LA.

activation of basal portions of the left ventricle, as previously mentioned. A diphasic (*RS*) ventricular complex is commonly recorded in the left lateral part; within the left superior pulmonary vein, an *rSr'* complex has been reported.[4]

Asynchronism of Left and Right Atrial P Waves: Quite often, a small positive deflection or a notch preceding the atrial complex is seen, which is easily recognized as being due to the activation of the right atrium. The timing of the intrinsicoid deflection of the P waves within the left atrium has been found to vary depending upon the higher or lower location of the recording electrode. The same fact has been observed in the right atrium.[2] Reviewing the bibliography, Levine *et al.*[20] in normal cases reported asynchronism of 0.05 to 0.07 sec between the P wave recorded in the great cardiac vein and that of a simultaneous standard lead. Latour and Puech,[4] in various observations of intracavity potentials from the left atrium in cases of congenital defects, reported a similar asynchronism.

Our observations in the left atrium clearly indicate that, in every case studied, the intrinsicoid deflection of the atrial complex falls in the second half of the P wave in a simultaneously recorded lead 2 or 3, with variations in the same case of not more than 0.014 sec on pulling the catheter through the atrial cavity. For comparison, the inscription of the P wave inside the right atrium occurs in the first half of the P wave in the peripheral electrocardiogram. Figure 3 shows the normal asynchronism between right and left atrial activations in a case of atrial septal defect: in (A) the unipolar i.c. ECG is recorded from the right atrium (V-RA) and, in (B), from the left atrium (V-LA), with a simultaneous lead 2. The calculated asynchronism in this case was 0.035 sec, which matches quite closely the normal values found by direct electrocardiography.[17,18]

In the *first group* of our series, three cases with sinus rhythm had both right and left catheterization. Figure 4 shows the tracings of pressure and i.c. ECG with lead 2 from the right atrium (A), and from the left (B). The asynchronism between the two intracardiac P waves in these cases was found to vary between 0.04 and 0.075 sec with variations of from 0.009 to 0.014 sec in each single case. In this group, three other

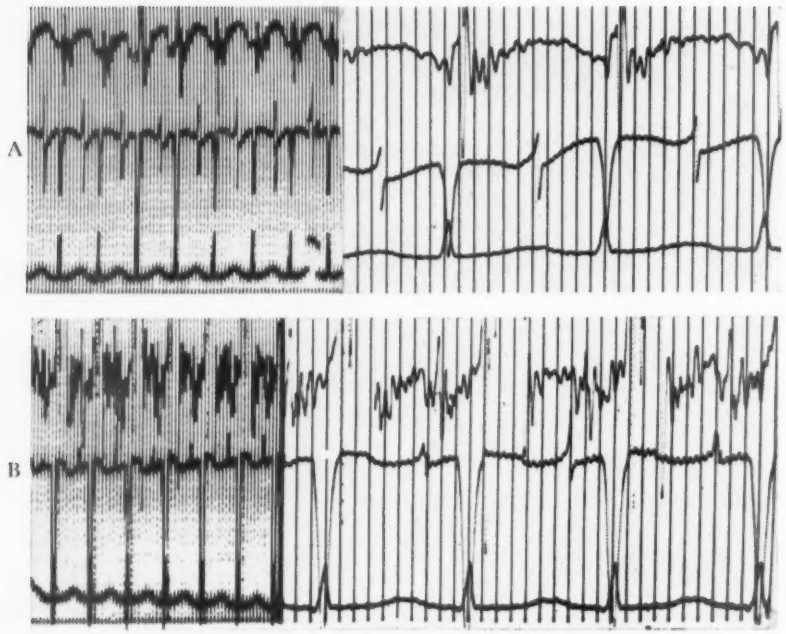


Fig. 5. Case of pure mitral insufficiency. This was the only case presenting a tall, peaked P wave in the left ventricle. (A). Left atrial pressure, lead V-LA, and lead 2. (B). Lead V-LV, and lead 2. Film speeds: 25 and 100 mm/sec. The P-R interval was 0.120 sec in the atrium and 0.085 sec in the ventricle. The P-R interval of lead 2 cannot be accurately calculated on account of the tachycardia and superimposition of T and P waves. The peripheral ECG at rest presented a 1st degree A-V block with a P-R interval of 0.230 sec.

cases with sinus rhythm and predominant mitral stenosis underwent left heart catheterization only. In the total number of six, the asynchronism between the P from the left atrium and that of a simultaneous lead 2 was calculated from 0.05 and 0.09 sec with variations of less than 0.02 sec in each single case. Comparing the two sets of figures, it is evident that the asynchronism is increased by the late inscription of the intrinsicoid deflection of the P wave in lead V-LA. In spite of the above variations, our values correlate with those obtained through direct epicardial leads in a similar group of patients.[18]

The degree of asynchronism (time of inscription of the intrinsicoid deflection) is inversely proportional to the voltage of the P wave in the left atrium: as a rule, greater voltage is accompanied by lesser asynchronism, and vice versa. Puech[37] first emphasized this point through the use of direct and esophageal leads. Figure 5 illustrates a striking example of asynchronism for the P in the left atrium and for that in the ventricle. The patient presented pure mitral insufficiency (6 mm of systolic rise in left atrial pressure).

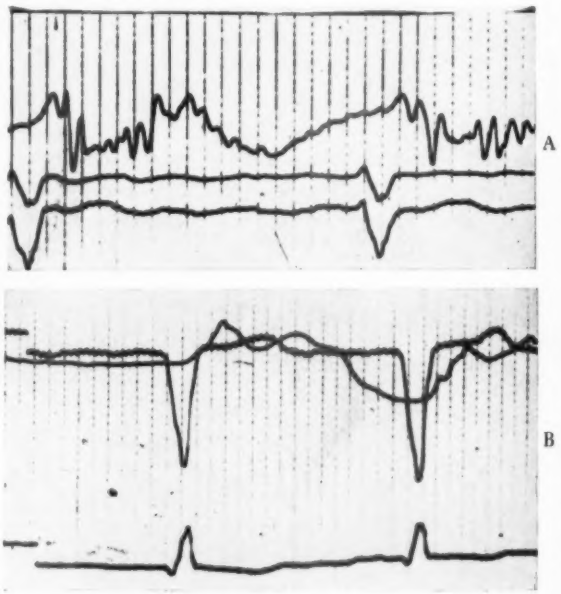


Fig. 6. Case of left ventricular hypertrophy and atrial fibrillation. (A) Right atrial pressure, lead V_1 and V-RA. (B) Lead V-LA, left atrial pressure curve, and lead V_6. The standardization is indicated at the beginning of the tracing. Film speed: 100 mm/sec. In both tracings, no evidence of coordinated atrial activity can be seen. In (A) lead V_1 and V-RA are similar. In (B), increased voltage of the ventricular complex.

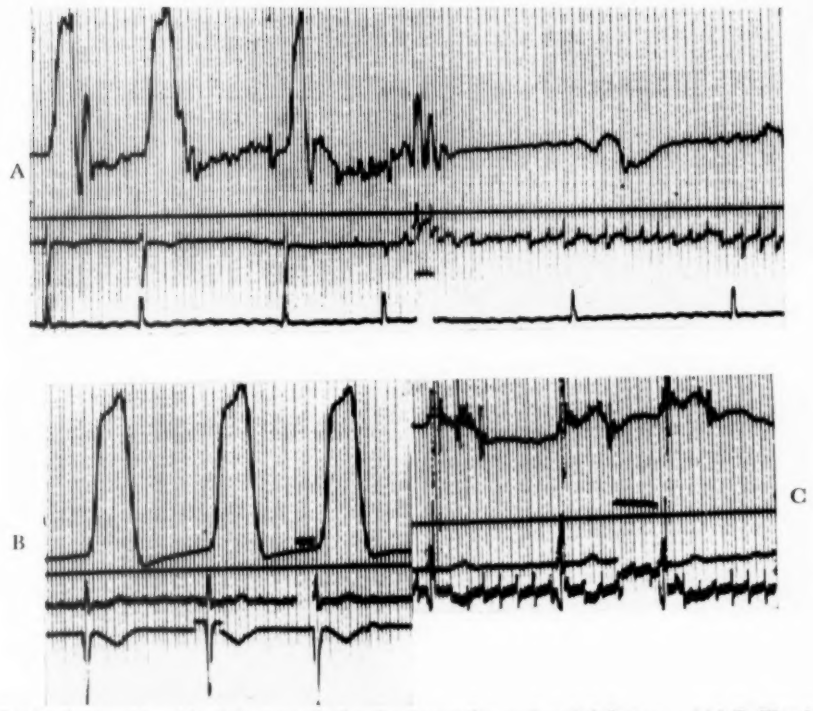


Fig. 7. Case of mitral stenosis with right ventricular hypertrophy and atrial flutter. (A) Pullback from the right ventricle to the right atrium. From above: pressure, intracardiac unipolar lead, and lead 2. Film speed: 25 mm/sec. A sudden change of intracardiac pressure pattern and i.c. ECG marks the crossing of the A-V valve by the catheter; flutter waves appear as soon as the catheter is pulled in the atrium. (B) and (C) Pressure curve with lead 2 and i.c. V-lead, from the left ventricle and atrium, respectively. In (B), V-LV presented a normal ventricular complex and no atrial activity, while the latter is seen in V-LA ("f" waves).

Tall peaked P waves are recorded in the left ventricle (B) with the same characteristics of the P in the left atrium (A). The only difference is a P-R interval of 0.12 sec in the atrium and of 0.085 sec in the ventricle; the P-R interval of the simultaneous lead 2 cannot be accurately calculated on account of the tachycardia and resultant superimposition of T and P waves. The peripheral ECG at rest presented a first degree A-V block with a P-R interval of 0.23 sec.

Amplitude and Duration of P Wave: Comparison of the voltage of the P waves in either atrium with that of the P waves in a standard lead revealed no correlation; in the latter, the height of the P depends upon the axis of P in either the frontal (extremity leads) or the horizontal plane (precordial leads). The so-called "P mitrale" is due to a left axis deviation of the second component (positive in lead 1, negative in lead 3), while the initial right atrial half of the P has a normal axis. As for the precordial leads, Hecht[38] first reported that, in almost all cases of mitral stenosis, a diphasic P wave is present in V_1, even when P is normal in the standard leads, and that its negative part is due to the vector of left atrial depolarization. Thus, it is evident that the width of the P wave in the peripheral electrocardiogram depends upon the asynchronism between right and left atrial depolarization, as shown by intracardiac leads from both atria.

We were unable to find any relationship between the height of the P waves in the left atrium and the level of left atrial pressures or the calculated value of mitral valve area or resistance. As known, previous observers failed to show any such correlation between hemodynamics of mitral stenosis and voltage of the P wave in the standard[39] or direct epicardial leads.[18] Reynolds, in trying to explain this discrepancy, expressed the hypothesis that high voltage of the left atrial P indicates a well-functioning left atrium and vice versa. This "func-

tional" element (which is necessarily connected with structural conditions) would explain the asynchronism and the tall P waves in the left cavity leads of Figure 5.

Findings in Atrial Fibrillation and Flutter: In our series, three cases with atrial fibrillation were studied by both right and left heart catheterization. Figure 6 shows in (A) the tracing of right atrial pressure, V_1 and V-RA; in (B), left atrial pressure, V-LA, and V_6. The electrical activity recorded in both atria is represented by polymorph and irregular waves of "désynchronisation rapide."[40] Double catheterization was also performed in 2 cases of atrial flutter. Flutter waves are seen in the right atrium after a pullback from the ventricle (Figure 7A); the tracings from the left chambers show no atrial activity in the ventricle (Fig. 7B) while the atrial tracing (Fig. 7C) is similar to an esophageal lead.

Ventricular Complex: The ventricular complex, as already mentioned, presents a different pattern at various levels of the exploring electrode within the atrium. The changes of the QRS, ST, and T of clinical cases are secondary to those found in the ventricle and will be discussed below. Still, mention can be made that, in cases of left ventricular hypertrophy, increased voltage of the ventricular complex and QS or QR patterns according to the atrial level, were found. A late R is typical of the uppermost parts of the left atrium, being the expression of late activation of basilar portions of the hypertrophied left ventricle.

It should be kept in mind that the height of the deflections cannot be calculated in terms of absolute values because of the uncertain distance of the tip of the recording catheter from the en-

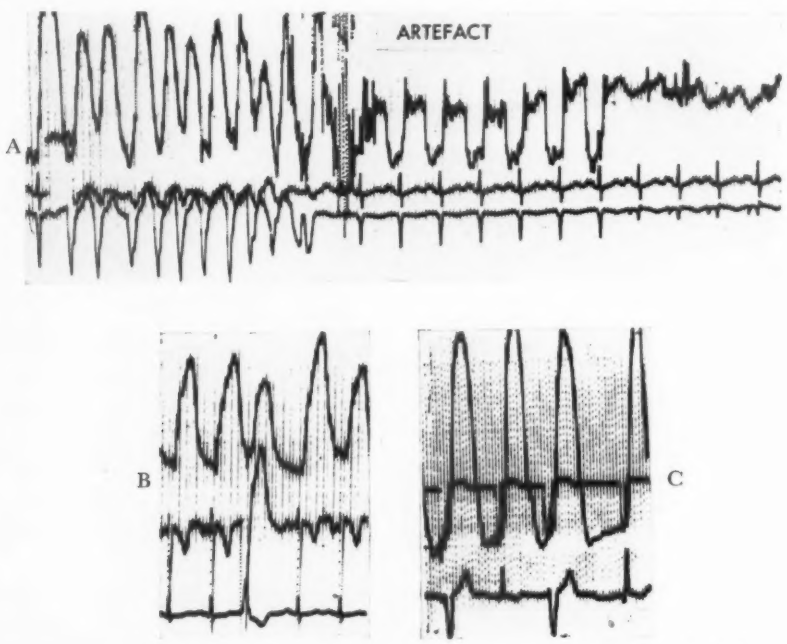


Fig. 8. Induced premature beats during catheterization. (A) Pullback tracing from the left ventricle to the left atrium. Pressure curve with lead 2 and intracardiac V-lead. The standardization is indicated at the beginning of the tracing, after the first normal ventricular complex. Following this, one can see a run of left ventricular premature beats followed by an artefact both in the pressure tracing and in the i.c. ECG (intermediate patterns between the tracings recorded in the ventricle [first beat] and in the atrium [last four beats]). This figure also demonstrates the ECG pattern of premature left ventricular beats in leads 2 and V-LV; in this lead, a broad QS pattern and secondary ST and T changes are recorded. (B) Right ventricular pressure, V-RV, and lead 2 of same case. The third beat is a premature right ventricular beat showing i.c. pattern of widened QS, and ST and T secondary changes. The similarity of the two i.c. unipolar leads for premature beats of the homologous ventricle is striking. The peripheral ECG presents a pattern similar to LBBB for RV premature beats, and to RBBB for LV beats. (C) Case of left ventricular hypertrophy with sagging ST in the left precordial leads. LV pressure curve, V-LV, and V_6. The first and third beat are LV premature beats. The pattern of the premature beats in V_6 is *rS* with secondary ST and T changes while, in V-LV, there are wider ventricular complexes. Film speed: 25 mm/sec.

docardial surface. As already said, in studies of intracardiac electrocardiography this fact represents an inevitable drawback, inherent to the catheter technique.

ELECTROCARDIOGRAM RECORDED WITHIN THE LEFT VENTRICLE

The deflections within the normal left ventricle consist of a positive P wave, a QS complex, and a negative T wave (Fig. 1). A distinct U wave was never found, in agreement with the observations of Sodi-Pallares.[9] The P wave, due to the low amplification used for intraventricular recording, was usually extremely small or flat. The only exception encountered was the case of mitral insufficiency; a possible explanation for it was already mentioned. In our laboratory, the technique of multiple pullbacks is currently used. With this maneuver, a progressive flattening of the T waves is observed, and the passage from one to the other chamber is usually evidenced by a sudden change in pattern from ventricular to atrial characteristics. This parallels a similar sudden change in the pressure curve. The same sharp difference of patterns is seen in pullback maneuvers in the right heart.

Attention should be paid to the proper technique: a noncontinuous traction on the catheter may bring about various artefacts. Figure 8A is such an example; one of the pullbacks, incorrectly performed in one patient, caused the appearance of an intermediate pattern in both the mechanical and electrical tracings, as compared to those recorded in the ventricular and atrial cavities.

Ventricular Premature Beats: Figure 8A also shows the configuration of left ventricular premature beats with the i.c. pattern of broad QS, and secondary ST and T changes. For comparison, in Figure 8B is shown the unipolar lead within the right ventricle (lead V-RV) for premature beats elicited through stimulation of the right endocardial surface by the exploring electrode. The similarity of the two intracardiac leads for premature beats arising from the homolateral ventricle is striking: in both instances, in fact, the activation wave of ventricular depolarization is moving away from the intracardiac exploring electrode. Consequently, an intracardiac rS pattern would be found in either ventricle for premature contractions originating in the contralateral ventricle.

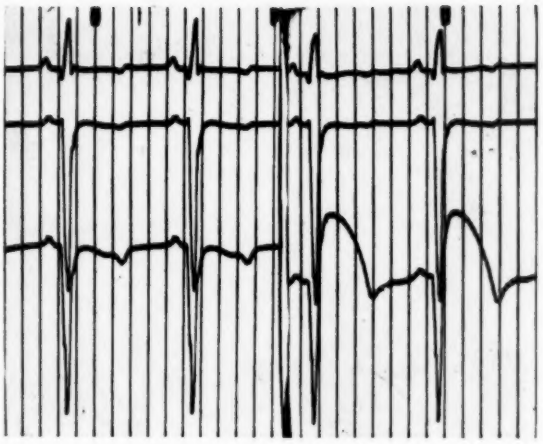


Fig. 9. Normal dog. From above: simultaneous lead 2, V-RV, and V-LV before and after experimental production of a monophasic wave of injury, by pressing the tip of an exploring catheter against the endocardial surface of the left ventricle. The monophasic wave is recorded only from the catheter inside the left ventricle while no changes are seen in either the right ventricle or lead 2. Film speed: 100 mm/sec.

In both figures, the same lead 2 simultaneously recorded illustrates a pattern similar to left bundle branch block for right ventricular premature beats, and to right bundle branch block for left ventricular beats. Figure 8C demonstrates premature contractions having an rS in V_6 and a broad QS in lead V-LV (beats 1 and 3) in a case of left ventricular hypertrophy with ST sagging in the left precordial leads; it is interesting to note, however, that the ST and T wave in the i.c. lead present no alteration as compared to beats 2 and 4.

Barker *et al.*[41] first pointed out the ventricular asynchronism occurring in premature beats artificially elicited through epicardial stimulation of either ventricle, thus laying the theoretic ground for Wilson's reversal of the conventional concept of bundle branch block.

Intracardiac Injury Currents: In 1936, Marcu,[42] followed by Loukomski and Guinodman[43] using standard leads, described the pattern of premature ventricular beats, obtained through experimental stimulation of the endocardium. All the subsequent observers recognized the sensitivity of the ventricular endocardium to mechanical stimulation by the catheter. If the

catheter tip presses against the endocardial surface for more than a few seconds, a monophasic wave of injury appears which is recorded only in the endocardial electrocardiogram and is not associated with ST deviation in simultaneous precordial, standard, or intracardiac leads from other chambers. This point is illustrated in Figure 9, where simultaneous lead 2, V-RV, and V-LV are recorded before and after an injury wave is produced by pressing the catheter tip against the left ventricular endocardium of a dog. Additional evidence indicates that the intracardiac injury pattern is due to a minimal and strictly localized injury; in fact, it disappears abruptly on withdrawal of the catheter.

Unmistakably, these facts have a bearing on clinical electrocardiography in regard to the evaluation of patterns of subendocardial injury and ischemia. In this connection, it should be noted that, in spite of injury currents on the endocardial surface, the peripheral ECG still remained "normal." This fact, which indicates the limited extension of the "injured" area, may explain the possible occurrence of a "tracing within normal limits" in the presence of heart disease. With this in mind, one may question how "localized" is a pattern of injury or ischemia recorded in the peripheral ECG. Of practical significance is a "pathognomonic sign" in Ebstein's disease, first described by Cisneros *et al.*[44] and recently confirmed by Hernandez *et al.*[45] It consists of a ventricular monophasic wave of injury produced by pressing the catheter against the septum in a chamber within which the pressure curve has an atrial pattern: this would indicate the existence of ventricular muscle above the tricuspid valve, a malformation which is characteristic of Ebstein's anomaly.

Comparison of Left Ventricular ECG and Left Precordial Leads: Interesting observations were

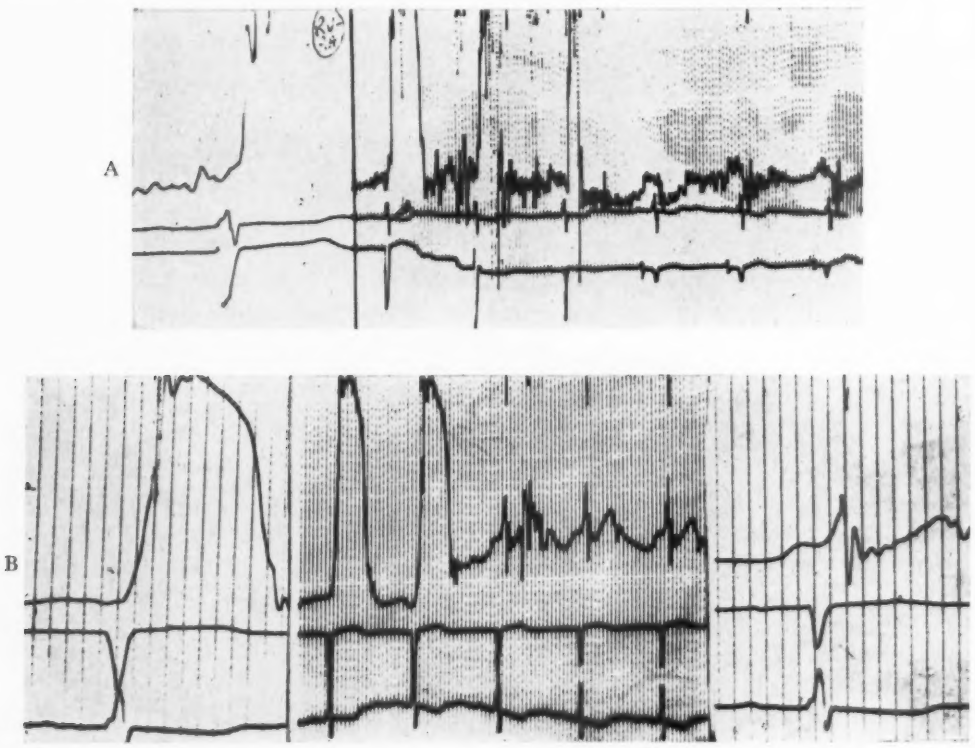


Fig. 10. Case of pure right ventricular hypertrophy and "digitalis effect." (A) RV-RA pullback tracing. Pressure curve, lead V_5, and i.c. V-lead. In the first part of the tracing, the film speed was 100 mm/sec; in the rest, 25 mm/sec. The sudden change of the intracardiac pressure curve coincides with a sudden change of the i.c. ECG from a ventricular to an atrial pattern. (B) LV-LA pullback tracing. Pressure curve, i.c. V-lead, and V_5. In the first and last part of the tracing, the film speed is 100 mm/sec; in the middle part, it is 25 mm/sec. Observe the changes of both i.c. tracings (pressure curve and ECG) upon pulling the catheter across the mitral valve. In all four cardiac chambers the same ST changes are seen.

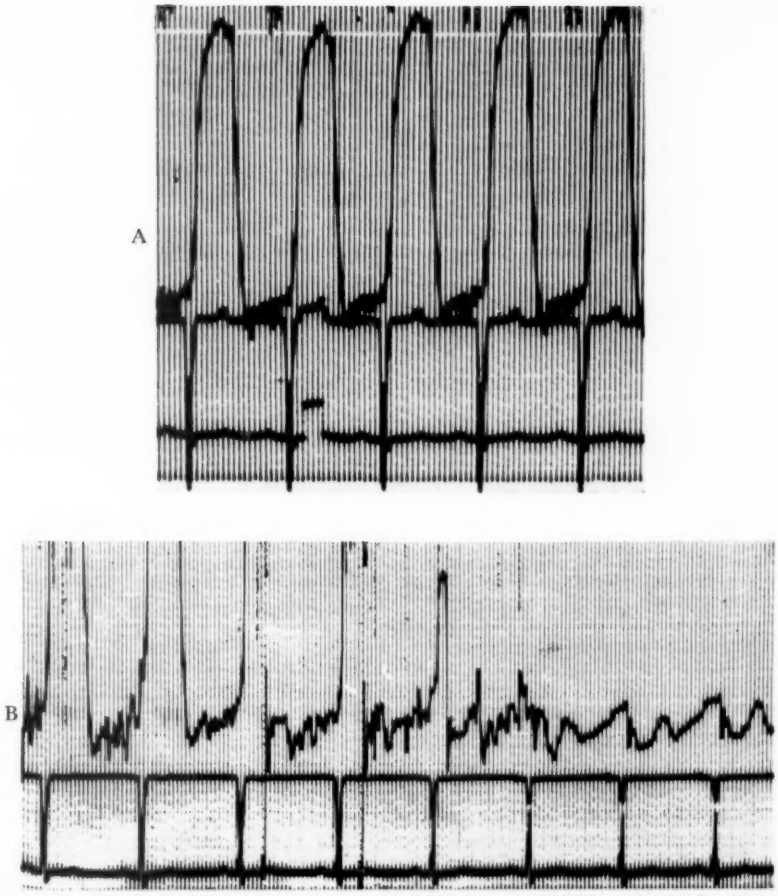


Fig. 11. Case of isolated left ventricular hypertrophy. (A) LV pressure, V-LV, and lead 2; film speed 25 mm/sec. The standardization is presented after the second beat. Increased voltage of i.c. QS and positive T waves. (B) Same case, LV-LA pullback tracing. Pressure curve, i.c. V-lead, and lead 2. Progressive flattening of the intracardiac T waves and sharp change from ventricular to atrial pattern of i.c. ECG.

obtained comparing the unipolar left ventricular lead with the chest leads overlying the left ventricle.

A normal V-LV lead was recorded only in the first group of our cases, where the peripheral electrocardiogram was normal or showed evidence of isolated right ventricular hypertrophy. Figure 7B is such an example of a normal i.c. ECG. One of these cases presented evidence of pure right ventricular hypertrophy and "digitalis effect"; in intracardiac V-leads, a similar ST pattern was found in all four cardiac chambers (Fig. 10A, B). When left ventricular hypertrophy, or both right and left hypertrophy were present, increased voltage of QRS was found (Fig. 11A). In Figure 11B the pullback is shown.

Intracardiac T Waves: The direction of the intracardiac T waves in cases with a normal left ventricle was always found to be discordant with the polarity of the T waves recorded over the left precordium. A similar discordance, though in the opposite direction, was found in cases of left ventricular hypertrophy or "strain" (Fig. 12). However, the intra- and extracardiac unipolar leads of the left ventricle are not strictly comparable, as shown by Figure 13, where the ECG was recorded within the left ventricle in the same case of Figure 11. While in the latter a positive T wave without ST alterations is recorded in V-LV, in the former there is an evident sagging of the ST segment with a negative-positive intracardiac T wave. Although this could be explained by a different orientation of the tip of the catheter (toward the apex in one instance and toward the base in the other), we were unable to

prove this point on account of the transparency of the catheter. However, a final conclusion requires further investigation, especially in view of some recent experimental work on the repolarization process of the normal heart.[46]

Another tracing presented a special interest (Fig. 14). It was recorded in a case of mitral stenosis and insufficiency with atrial fibrillation and left ventricular hypertrophy. No ST or T changes were observed in the left ventricle while they appeared as soon as the catheter was pulled in the atrium across the mitral valve. At the same time, the ventricular complex still had a high voltage inside of the left atrium, such as was never found in other cases. We have no explanation, at present, of this tracing.

Positive T waves were observed within the left ventricle in a case of atrial septal defect (Fig. 15)

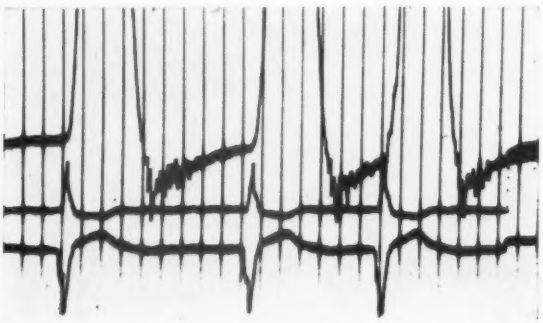


Fig. 12. Case of LV hypertrophy and "strain." Left ventricular pressure, lead 2, and V-LV. The calibration is at the end of the tracing; film speed 100 mm/sec. Upright displacement of the ST segment is recorded in the i.c. V-lead.

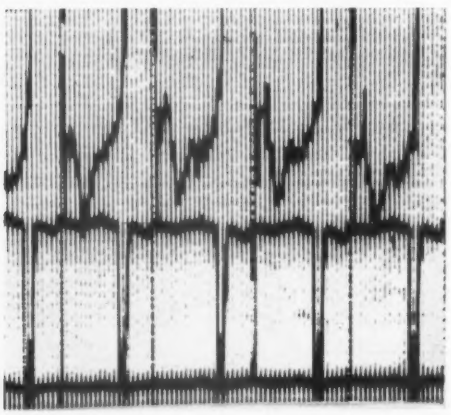


Fig. 13. Same case as Figure 11. LV pressure (partly cut off), V-LV, and lead 2; film speed 25 mm/sec. Evident sagging of ST and negative-positive T wave in lead V-LV.

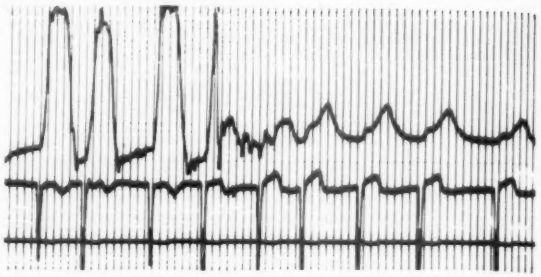
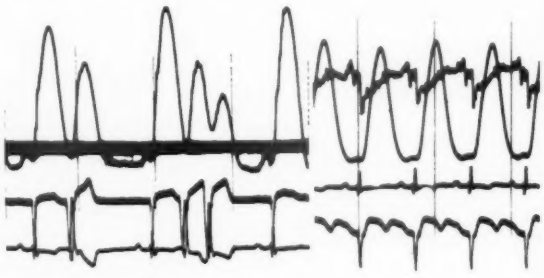


Fig. 14. Case of mitral stenosis and insufficiency with atrial fibrillation and left ventricular hypertrophy. LV-LA pullback tracing. Pressure curve, i.c. V-lead, and lead 2; film speed: 50 mm/sec. In the pressure tracing, there is a diastolic gradient of 7 mm Hg across the mitral valve and a systolic elevation of 7 mm Hg within the left atrium. The intracardiac V-lead presents a negative, symmetrical T-wave and no ST changes within the ventricle. Upon crossing the A-V valve, sudden upright displacement of the ST and positive-negative T waves appear, which are opposite in direction to the ST and T waves of the left precordial leads. There is the same high voltage of the QS in both the ventricle and the atrium.



A B

Fig. 15. Case of atrial septal defect. (A) Pressure curve and i.c. V-lead within the left ventricle with lead 2 at the bottom. V-LV shows a QS pattern with positive T waves; premature LV beats are seen (beats 2, 4, and 5) with broadened QS and secondary changes of ST and T. These, however, occur in the same sense of beat 1, 3, and 6. There is a pattern of RBBB in lead 2 for the LV premature beats. (B) Pressure tracing, lead 2, and V-RV.

and in a case of primary pulmonary hypertension (Fig. 16), both submitted to right and left heart catheterization. In the peripheral ECG, a qR pattern lasting less than 0.10 sec, sagging ST and negative T wave were present in right precordial leads, while a normal tracing was recorded in V_5 and V_6.

Initial Positivity (rS Pattern) in Left Ventricle: The tracing recorded during a pullback (Fig. 16A) shows an *rS* pattern within the left ventricle. In other cases, a similar initial positivity was frequently recorded in lead V-LV following a run of premature ventricular beats. In addition, we

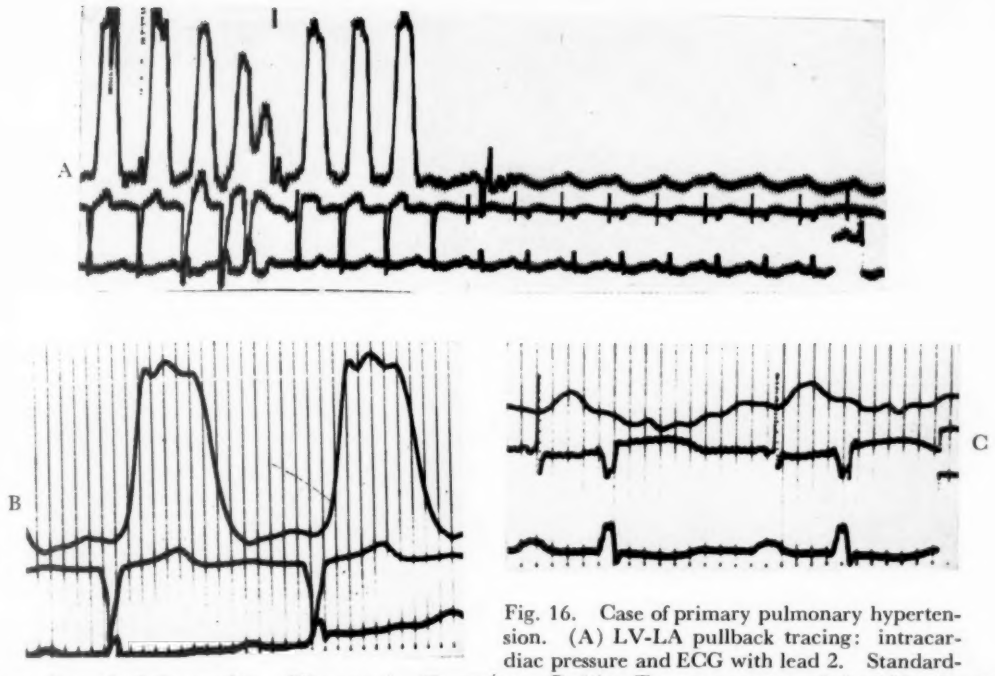


Fig. 16. Case of primary pulmonary hypertension. (A) LV-LA pullback tracing: intracardiac pressure and ECG with lead 2. Standardization at the end of the tracing. Film speed: 25 mm/sec. Positive T waves are recorded within the ventricle. Beats 3, 4, and 5 are LV premature beats; the following beat presents an *RS* pattern in V-LV. Sharp changes of both i.c. pressure and ECG occur upon crossing of the mitral valve. (B) and (C) show the same tracings at higher speed (100 mm/sec). In (C) the amplification was increased; the small positive deflection, preceding the i.c. P wave and simultaneous with the first half of the P wave in lead 2, represents the activation of the right atrium. ST and T changes are opposite to those in lead 2.

had two observations of an *rS* pattern recorded during pullback maneuvers, just prior to crossing of the mitral valve. Neither of the two cases fulfilled the criteria of incomplete left bundle branch block as set by Sodi-Pallares.[9]

Other authors recorded a positive wave within the left ventricle. An *RS* pattern was recorded by Zimmerman.[10, Figs. 4 and 5] A small positive initial deflection was reported both in a normal case and in a case with left ventricular hypertrophy by Coelho.[11, Figs. 18 and 24] Mas *et al.*[13] noticed *rS* in the mid-section of the left ventricle, but stated that it is more commonly seen after premature beats. Recently, Latour and Puech[4] reported three cases with an *rS* or *qrS* pattern in the left ventricle in the absence of intraventricular conduction disturbance. Finally, Rodriguez *et al.*[47] occasionally found a small *r* in high portions of the left ventricle of normal dogs.

The interpretation of this initial positivity inside the left ventricle still remains controversial. According to Sodi-Pallares,[26] this *initial r* could be explained by activation of the uppermost part

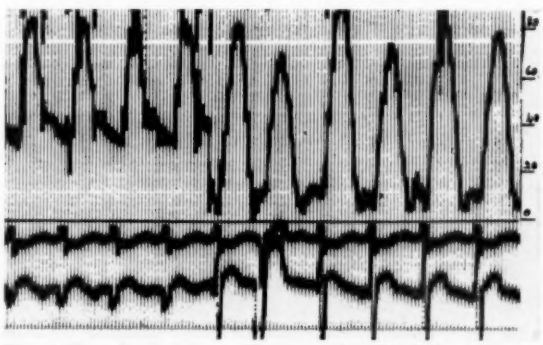


Fig. 16D. Same case. Tracing of a PA-RV pullback: pressure tracing, lead 2, and i.c. V-lead. Sharp changes in pattern of the i.c. tracings (pressure curve and ECG) occur upon crossing the pulmonic valve. Tall R is seen inside the right ventricle together with ST and T changes in the opposite direction of these of lead 2.

of the septum, or depolarization of a papillary muscle transmitted to the upper part of the left ventricular cavity. The *rS* pattern following left ventricular premature beats could be explained by a transient conduction disturbance produced by pressure of the catheter tip on the endocardium.

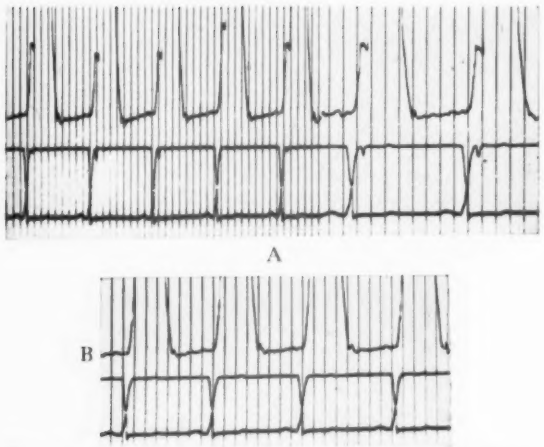


Fig. 17. Example of artefact. (A) Pressure curve, V-LV, and lead 2. A notching in the ascending limb of the pressure curve and a negative deflection after the i.c. QS are visible both at low and higher speeds. (B) Prompt disappearance of the artefact in both mechanical and electrical tracing is obtained upon slight withdrawal of the catheter.

Artefacts: A last pattern, recorded within the left ventricle, is illustrated in Figure 17. In (A) the pressure curve presents a notching in the ascending limb, while the i.c. ECG presents a negative deflection just following the ventricular complex. It is apparent that this represents an artefact, as shown by its prompt disappearance upon withdrawal of the catheter (B). Indeed, there is no other explanation for a deflection occurring in the absolute refractory period.

Summary

Observations are reported of intracardiac electrocardiography recorded during left heart catheterization, performed by the direct transthoracic puncture of the left atrium.

The report deals with 14 cases of rheumatic mitral or aortic valvular lesions, and 1 case of syphilitic aortic insufficiency. Three other cases were discarded because of failure of the catheter to pass through the mitral valve.

In eight cases catheterization of the right chambers was also performed with recording of intracardiac potentials. Right and left heart catheterizations and i.c. ECGs obtained in a case of atrial septal defect and one case of primary pulmonary hypertension are also presented.

The maneuver of multiple pullbacks was used. Attention is called to the proper technique so as to prevent artefacts.

When normal sinus rhythm is present, the intracardiac P wave in the left atrium falls in the second part of a simultaneously recorded standard lead P. The asynchronism between the intracardiac and peripheral P waves was found to vary between 0.05 and 0.09 sec in cases with predominant mitral stenosis, with variations of less than 0.02 sec in a single case. This increased asynchronism is due to the late inscription of the intrinsicoid deflection of the P wave in the left atrium, as shown by the findings in three cases in which right and left heart catheterizations were performed. The degree of asynchronism was found to be inversely proportional to the voltage of the intracardiac P wave.

No correlation was seen between the voltage of the P wave recorded in either atrium and the P in a standard lead. No relationship was found between the P wave inside of the left atrium and the values of atrial pressure, or calculated mitral valve area or resistance.

In cases of atrial fibrillation, polymorph and irregular waves were recorded in both atria. In atrial flutter, "f" waves were recorded.

The ventricular complex within the left atrium was strictly related to the QRS as recorded within the left ventricle.

The P waves inside the ventricle were normally flat; only one exception was encountered.

In atrial fibrillation or flutter, no atrial activity was recorded in either ventricle. The patterns of premature ventricular beats and of subendocardial injury are presented. Normal left ventricular complexes were recorded in cases of isolated right ventricular hypertrophy. In cases of left ventricular hypertrophy, on the contrary, increased voltage of the intraventricular QRS was recorded.

ST and T wave changes were found in the presence of left ventricular hypertrophy or "strain." Comparison between intracardiac unipolar leads and left precordial leads was made; discordant points were presented and an explanation was attempted.

Occasional *rS* patterns within the left ventricle were observed and are discussed.

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The Morphology of Normal and Abnormal Pulse Waves Recorded Plethysmographically*

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IN A RECENT communication[1] a useful classification of the slow waves of the digital plethysmogram was presented in terms of amplitude and frequency and the effect of vascular disease on these waves was discussed. The purpose of the present report is to describe the effects of peripheral arterial disease on the configuration of the pulse wave as recorded plethysmographically.

HISTORICAL REVIEW

Numerous methods have been used to record indirectly peripheral arterial pulsations. Early instruments utilized air or fluid-filled bags which were applied directly over a single artery.[2–9] Later, volume changes were recorded with the aid of devices which completely surrounded the part.[10,11] Still later, recording oscillometers[12–14] and standardized plethysmographs[15] were employed. Other methods have utilized a metal capsule with a rubber or metal membrane,[16–19] carbon[20] and crystal microphones,[21,22] photoelectric cells,[23–28] thermal units,[29–31] condensers,[32,33] a strain gauge,[34] and vacuum tube oscillators.[35]

These instruments have all produced valuable scientific information, but each of them has had one or more disadvantages which have made it relatively unsuitable for clinical work. The various disadvantages include the following: (1) irregular and inconstant results were obtained; (2) standardization was either completely lacking or was inadequate; (3) volume changes were not recorded in absolute terms; (4) volume changes were not recorded in a linear fashion; (5) sufficient sensitivity was lacking; (6) the slow volume changes were not recorded.

In the past five years, standardized electronic recording instruments have been developed. The most recently described pneumoplethysmographs are versatile instruments of high sensitivity which are capable of recording accurately the pulse volume changes in a digit[36] or in a segment[37] of a limb. The plethysmograms produced with these instruments have been carefully studied and the following report is a comment upon the morphology of normal and abnormal pulse waves as recorded by these plethysmographs.

METHOD

Over 100 patients with varying degrees and types of vascular disease have been studied with the plethysmographic technic, and the tracings have been correlated with the presence and amount of arterial disease. These wave forms have been compared carefully with those obtained from normal subjects.

The patients were studied in a room with a temperature of 24° C plus or minus 1.5° and an air velocity which amounted ordinarily to less than eight feet per minute, but at no time exceeded 12 ft/min. The patients were dressed in a standard hospital gown, were covered with one light woolen blanket, and were examined lying supine.

Two plethysmographs were employed. One was for a digit and the other for a segment of the limb. The direct writing electronic digital plethysmograph[36] was standardized so that a 1 mm deflection on the paper represented 1 cu

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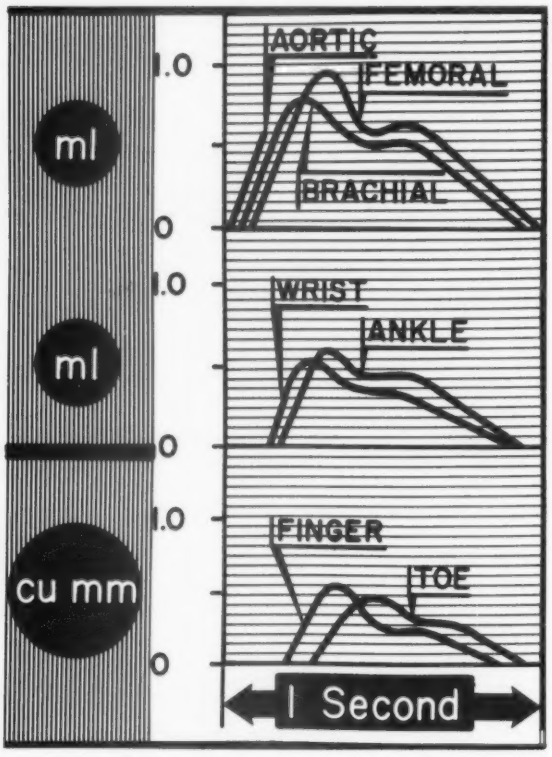

Fig. 1. Difference in timing of various peripheral pulse curves. (Figs. 1–5 reproduced from WINSOR, T.: *Peripheral Vascular Diseases—An Objective Approach*, Charles C Thomas, publisher.)

mm of volume change of the digit. A cup with a volume of 14 cu mm was employed and the volume of the digit sealed in the cup was always 4 cu mm.[36] The segmental limb plethysmograph[37] was standardized so that a 1 mm deflection on the paper represented a volume change of 100 cu mm in the segment of the limb. The instrument was employed at various positions on the extremities (i.e., above and below the elbow, at the wrist, in the femoral region, above and below the knee and at the ankle). The largest pulse waves were generally recorded just above diastolic pressure levels and it was from these waves that the amplitude measurements were made. Waves recorded at or just below diastolic pressure were analyzed for form.

The vasodilating technics used included: (1) a posterior tibial nerve block, (2) body heating, and (3) oral alcohol in a dose of two ounces of whiskey.[38]

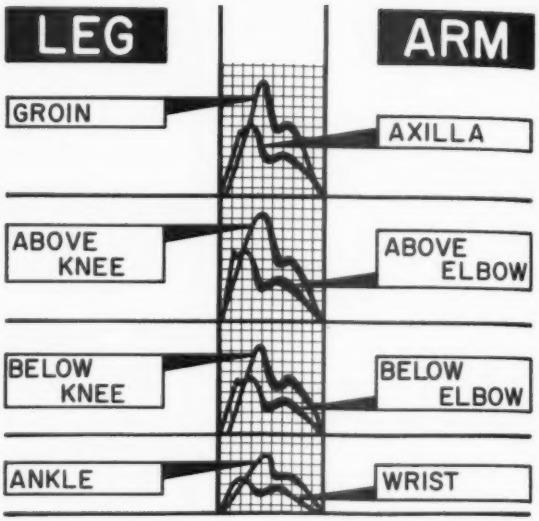

Fig. 2. Average difference in amplitude of normal plethysmographic curves at various peripheral positions.

RESULTS

Normal segmental plethysmographic waves from the brachium were similar in many respects to aortic curves as recorded by an intra-arterial needle. Waves recorded at the brachial position occurred somewhat later than the aortic curves but were similar in form (Fig. 1). The femoral curve was even later in onset than the brachial and the amplitude was somewhat higher (probably due to reflection waves from the periphery). The wrist and ankle pulses started later than the more central pulses and were lower in amplitude than the more centrally recorded waves (Fig. 2). In a comfortable environment the finger pulse was earlier and of greater amplitude than the toe pulse, while the ankle pulse was equal to or greater than the wrist pulse.

Various measurements may be used which aid in differentiating normal from abnormal pulse waves. These are: (1) crest time, (2) rate of rise of the anacrotic limb, (3) wave amplitude and pulsation ratio, (4) half rise time, (5) dicrotic notch, (6) rate of volume change, (7) harmonic analysis, (8) inclination time, and (9) pulse velocity.

Crest Time: The crest time (Fig. 3) is the duration from the onset of the wave to the crest or apex of the wave. Normally the crest time varies with the cycle length. The normal

values for the crest time and the per cent of the cycle length (i.e., crest time in seconds/cycle length in seconds × 100) are given in Table I. With obstructive arterial disease (aortic stenosis, arteriosclerosis obliterans, coarctation, etc.) the crest time becomes significantly prolonged and occupies a greater percentage of the total cycle length.

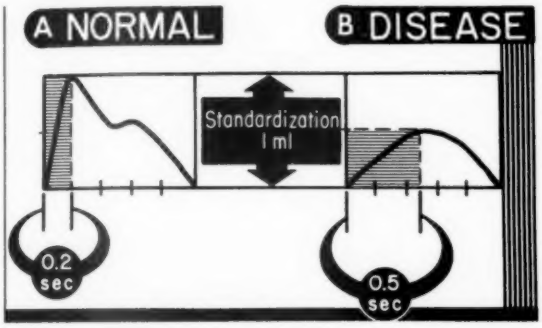

Fig. 3. The crest time is the duration of time from the onset of the wave to its peak or apex. The crest time becomes prolonged in patients with arterial obstructive disease (B) as compared to the normal patient (A).

Rate of Rise of Anacrotic Limb: This measurement (Fig. 4) is calculated by drawing a line parallel to the most rapidly rising portion of the anacrotic limb of a standardized pulse curve. The amount of rise of this line in one second is the rate of rise of the anacrotic limb. The normal values (30 subjects) for the rise rate of the ankle or wrist curves ranged from 4 to 10

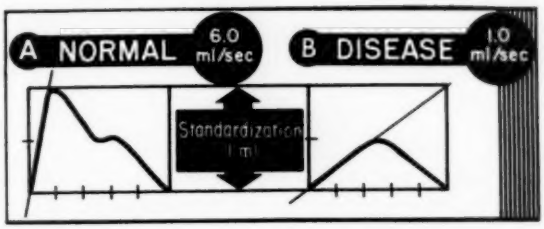

Fig. 4. The rate of rise (in ml/sec) of the anacrotic limb is slower in patients with arterial obstructive disease (B) than in normals (A).

ml/sec with an average of 6 (Fig. 4). Normally the rise rate varied with the amplitude, the pulse rate and with the proximity of the recording site to the aorta (i.e., it is more rapid at locations closer to the aorta).

Wave Amplitude and Pulsation Ratio: The average wave amplitude of normal pulse waves was greater at all cuff positions in the lower extremities than at comparable locations in the upper extremities (Table II). It therefore follows that the average pulsation ratio (i.e., lower extremity pulse amplitude divided by the upper extremity pulse amplitude) was greater than 1.0 in the normal subject if the pulses were compared at comparable areas of the extremities. Also, analysis of the records of 30 normal subjects revealed that the average pulse amplitude above the elbow was 4.0 per cent less than at the axilla and the amplitude below the elbow was 1.0 per cent greater than above the elbow. At the wrist the pulse am-

TABLE I*

Crest Time Expressed in Seconds and as the Per Cent of Cycle Length in Normal Individuals and in Patients with Arteriosclerotic Obliterative Disease in Pulses Recorded above the Knee, at the Ankle and at the Toe

	Above knee				Ankle				Toe			
	Normal		AOD†		Normal		AOD		Normal		AOD	
	Crest time	Cycle length (%)	Crest time	Cycle length (%)	Crest time	Cycle length (%)	Crest time	Cycle length (%)	Crest time	Cycle length (%)	Crest time	Cycle length (%)
Mean	0.23	30.5	0.29	35.9	0.22	29.5	0.26	31.5	0.20	25.7	0.36	41.7
Minimum	0.20	24.9	0.20	21.8	0.17	25.0	0.22	21.5	0.16	21.0	0.26	34.2
Maximum	0.26	44.4	0.40	51.3	0.25	34.4	0.32	43.0	0.26	31.3	0.56	49.9

* Reproduced from WINSOR, T.: *Peripheral Vascular Diseases—An Objective Approach*, Charles C Thomas, publisher.
† AOD: Arteriosclerotic obliterative disease.

TABLE II*

Normal Values (Mean and Extremes) for Pulse Wave Amplitude and Pulsation Ratios

		MEAN	EXTREMES
MILLILITERS	Above elbow	.7	.4-1.2
	Below elbow	.7	.4-1.1
	Wrist	.4	.2-.5
	Groin	1.8	1.2-2.9
	Above knee	1.5	.9-2.0
	Below knee	1.3	.9-1.9
	Ankle	.5	.3-.7
RATIOS	Above knee / Above elbow	2.1	.9-3.9
	Ankle / Wrist	1.6	.9-2.1

* Reproduced from WINSOR, T.: *Peripheral Vascular Diseases—An Objective Approach*, Charles C Thomas, publisher.

plitude was 52 per cent less than below the elbow. The pulse amplitude above the knee was 16 per cent less than that at the groin and the amplitude below the knee was 11 per cent less than above the knee. The pulse amplitude at the ankle was 59 per cent less than that below the knee.

Half Rise Time: The half rise time is the time necessary for the anacrotic limb to reach half of its total height. This measurement was prolonged in obstructive disease of the arterial tree and with slow heart rates. It should be noted that the half rise time is not necessarily prolonged in curves that have a prolonged crest time.

Dicrotic Notch: The dicrotic notch (Fig. 5) was present in normal digital pulse waves (30 subjects). This feature of the normal pulse tracing disappears in pulse tracings below an obstruction in patients with arterial obstructive disease (30 patients with arteriosclerosis obliterans).

Rate of Volume Change: The rate of volume change of a pulse wave is another measure of

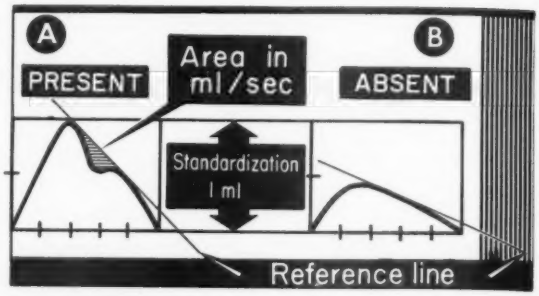

Fig. 5. The dicrotic notch is seen in the normal tracing (A). In the patient with diseased arteries (B) the dicrotic notch disappears.

the state of health of the arterial tree. This can be measured by dividing the pulse wave into equal time increments and measuring the volume change of each increment. These volume changes are then plotted against time. The rate of volume change was decreased in patients with obstructive arterial disease (five normals and five abnormal patients).

Harmonic Analysis: Harmonic wave analysis (Fourier analysis) may be derived manually or by electronic computers. The magnitude and direction of the harmonic components which make up the waves may be shown as polar graphs. In patients with arterial disease the second, third, and fourth harmonic vectors were of low magnitude and they showed an abnormal phase shift when compared to normal values (20 normals and 20 abnormal patients).

Inclination Time: The inclination time is derived by drawing a tangent to the steepest part of the anacrotic limb and then calculating the duration between points where the tangent intercepts the base level and the apex of the curve. In Lund's series[39] the upper limit of the normal value for the inclination time of the toe pulse was found to be 0.13 sec and in the finger 0.12 sec (the method of standardization in this series is not clear). Lund found that these values became prolonged in patients with an obstruction in the arterial tree. In our series the upper limit of normal for 30 subjects of the inclination time in the standardized record was 0.16 sec in the finger and 0.20 sec in the toe pulse. In 30 cases of arterial obstructive disease of the lower extremity there was no value less than 0.24 sec while 87 per cent

were 0.30 sec or longer and 67 per cent were 0.40 sec or longer.

Pulse Velocity: The pulse velocity may be measured by using a segmental plethysmograph in association with the phonocardiogram. The velocity (from the heart to the ankle and/or wrist) was increased after exercise, with body heating, after alcohol ingestion and in high output states (i.e., anemia, pregnancy, thyrotoxicosis, etc.), while it was decreased in hypothyroidism, shock, decreased cardiac output, and in patients with severe arterial obstruction. The pulse velocity was slow in 10 patients with diffuse, severe arteriosclerosis obliterans compared with 10 normal subjects.

Discussion

The measurements which have been described are used to extract as much information as possible from the plethysmographic study. By carefully studying the configuration of the pulse waves in the manner described above one can arrive at certain conclusions which are of aid in distinguishing between the healthy and the diseased arterial tree. In order to see how these measurements may be used we shall briefly discuss several disease states and note which changes occur.

(1) *Arterial Obstructive Disease:* This includes aortic stenosis, aortic coarctation, and peripheral arterial obstructions. Proximal to the obstruction the pulse wave is peaked and increased in amplitude, probably secondary to reflection waves from the obstruction. Below the obstruction the waves are low, rounded, have a delayed crest time, a delayed inclination time, a slow rate of volume change, a delayed half rise time, a decreased pulse velocity, and the second, third, and fourth harmonic vectors show an abnormal phase shift. All of these measurements seem to be more severely changed when the obstruction is a peripheral one (arteriosclerosis obliterans) than when the obstruction is centrally located (aortic valvular stenosis and coarctation of the aorta).

(2) *Aortic Regurgitation:* The pulse wave is tall, the catacrotic limb returns sharply to the base line and is often flat.

(3) *Hyperthyroidism:* The waves are increased in amplitude and the pulse velocity is increased. The catacrotic limb falls to the base line rapidly.

(4) *Aortic Aneurysm:* The wave forms are variable because of the difference in the nature of the aneurysm but a high percentage of patients have an increased amplitude of pulsation below the level of the aneurysm. A low amplitude, delayed crest time, and other evidence of obstruction may occur if the aneurysm is of an obstructive nature; however, this is not the rule.

Summary

An analysis of the morphology of the pulse waves from limbs or digits gives clinical information concerning arterial obstructions, and possibly hyperthyroidism, aortic regurgitation and aortic aneurysms.

The various simple measurements used in studying the waves include the crest time, the rate of rise time, the pulse amplitude, the half rise time, the presence or absence of the dicrotic notch, the rate of volume change, harmonic analysis, inclination time, and pulse velocity.

If properly considered the arterial pulse curve gives significant information relative to the physical state of the arteries and may be used to follow treatment of the cause of arterial disease.

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Review

Physiopathologic Study (Clinical and Experimental) of the Tricuspid Valve*

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IN 1836 Benson[2] noted some characteristics of the venous pressure pulse in a case of tricuspid insufficiency confirmed by autopsy. The French physician Duroziez[7,8] described in 1868 the symptomatology of tricuspid insufficiency in congestive cardiac insufficiency consisting of a xiphoid systolic murmur, high venous pressure, enlarged right auricle, distended neck veins with systolic pulsation, cyanosis of cheeks and lips, large liver and hepatic pulse; later, ascites and edema of the lower limbs develop. The venous pressure reaches its maximum during ventricular systole, due mainly to the transmitted pressure from the ventricle.

To these clinical findings the Mexican author Ribero Carvallo[4,5] has added a new sign—increase in systolic murmur in the tricuspid area during deep breathing. We have found this sign in the absence of tricuspid insufficiency, although it does exist in a number of patients with tricuspid insufficiency. A systolic murmur at the apex (spreading toward the sternum), often so very difficult to interpret if it occurs, is also a sign of tricuspid insufficiency.

The electrocardiogram can also present certain signs suggesting the presence of tricuspid insufficiency—low QRS, delay in the intrinsicoid deflection in V_1 and, occasionally, rsR′ in V_1.

Findings suggesting tricuspid stenosis include marked presystolic pulsation in the veins of the neck, enlargement of the liver, and ascites with slight edema of the lower limbs. A tricuspid diastolic murmur is rare. Tricuspid stenosis frequently escapes clinical diagnosis. Tricuspid insufficiency is very frequent in congestive cardiac insufficiency, but the clinical symptoms are not always sufficient to permit diagnosis.

PHLEBOGRAPHY

Long experience has proved, since the beginning of the century, that the phlebogram is valuable in the diagnosis and physiopathologic interpretation of tricuspid insufficiency and stenosis. A high systolic pulse, registered in the jugular vein, has long been recognized as a sign of tricuspid regurgitation. The A wave disappears if there is atrial fibrillation but after the C wave the curve does not descend, and there is no systolic collapse. This is replaced by a systolic wave "en plateau," coinciding with the regurgitation which occupies the whole duration of the systole; the collapse takes place in full diastole.

Gerhardt[12] reported several types of systolic regurgitation waves in the phlebograms of patients suffering from tricuspid insufficiency. He showed that this wave could present its maximum elevation at any phase of systole. Mackenzie,[27] Wiggers,[37] Groedel,[15] Messer,[30] Trainito and Maizzi,[35] and more recently Müller and Shillingford[31] have published phlebograms of patients suffering from tricuspid insufficiency. Messer *et al.*,[30] from their interpretation of the tracings of the jugular pressure, draw conclusions which are very important for differential diagnosis. If the regurgitation wave is early and "en

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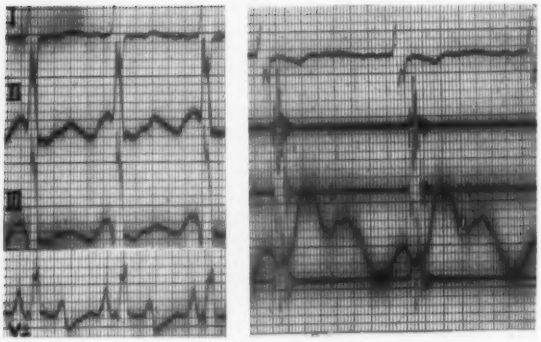


Fig. 1. Phlebogram of functional tricuspid insufficiency. *Left*, ECG—atrial flutter. *Right*, phonocardiogram, phlebogram.

plateau," this is proof of functional tricuspid insufficiency (Fig. 1). On the other hand, if the regurgitation wave is late in relation to the C wave, then it is a case of organic disease (stenosis or insufficiency and stenosis together) (Fig. 2). The factors responsible for the delay in the systolic regurgitation in organic disease are the incomplete filling of the right ventricle due to valvular obstruction, and a decrease in the speed of regurgitation caused by high atrial pressure associated with the valvular obstruction. Nevertheless, the phlebogram is not always sufficient to permit the diagnosis of tricuspid disease. Auricular stasis may present a wave "en plateau" often very difficult to distinguish from that of tricuspid insufficiency.

Abnormal Right Atrial Curves

It is necessary to study the right atrial curves and to take into account their various aspects in determining the hemodynamic alterations of organic tricuspid disease and of functional tricuspid insufficiency. Notable contributions of many authors[6,11,13,19,20,32,36,38] helped to establish the bases for the hemodynamic diagnosis of tricuspid stenosis. Bloomfield *et al.*[3] described the curves of right atrial pressure in eight cases of tricuspid insufficiency and showed that the normal systolic decline was replaced by a wave "en plateau" which occupied the whole of systole up to isometric relaxation; the pressure was higher than during the presystolic interval. They stressed that if there was congestive cardiac insufficiency without tricuspid insufficiency, the systolic fall corresponding to the lowering of the base of the auricle was very marked. Similar

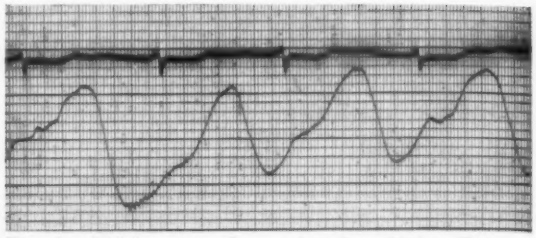


Fig. 2. Phlebogram of organic tricuspid insufficiency.

observations were published by Lagerlöf and Werkö.[23] McCord and Blount[28,29] noted a systole wave which often increased with exertion in four patients suffering from rheumatic heart disease and presenting clinical symptoms of tricuspid regurgitation. They believed the amplitude of this wave was an index of the severity of the regurgitation. Of 22 catheterized patients with mitral stenosis Lukas *et al.*[26] observed tricuspid insufficiency in 8, and of these only one had been diagnosed clinically. Ferrer *et al.*[10] published details of 8 cases of tricuspid insufficiency without clinical symptoms which might have suggested the diagnosis later brought to light by the hemodynamic examination. The same authors[11] have described one case of tricuspid stenosis confirmed by autopsy and another case of tricuspid disease in both of which the diagnosis could only have been made by hemodynamic examination. Müller and Shillingford[31] observed phenomena similar to that of McCord and Blount and, in addition, systolic regurgitation during deep breathing. Sepúlveda *et al.*[34] published a series of 60 cases in which the right atrial curve had the characteristics of tricuspid insufficiency. Clinical diagnosis had been established in only 23 of the cases.

We have been studying this problem for several years. Our present state of knowledge of tricuspid valve disease is the result of a study of right heart catheterization of 620 patients suffering from mitral disease. We have also carried out studies in 50 dogs with experimental tricuspid insufficiency during normal rhythm and during auricular and ventricular arrhythmias.

Normal Atrial Curves

On the normal curve (Fig. 3 with the speed of 25 mm/sec) three waves are observed—A, C, V— and two depressions, systolic and diastolic—

x,y. The A wave corresponds to the atrial systole. C corresponds to the closure of the tricuspid valve and to its bulging into the atrial cavity; it appears 0.08 second after the R wave of the electrocardiogram and indicates the beginning of ventricular systole. V corresponds to the filling of the atrium (stasis wave).

The atrial pressure falls during the course of the ventricular systole (*x*); this depression corresponds to the lowering of the base of the atrium and the relaxation of the atrial walls. The opening of the tricuspid valve corresponds to the *y* depression. The *x* depression is deeper than the *y* depression. In pulmonary hypertension the A wave can become very high and the descent of *x* becomes sharper. Figure 4 shows another aspect of the normal atrial curve taken at the speed of 75 mm/sec.

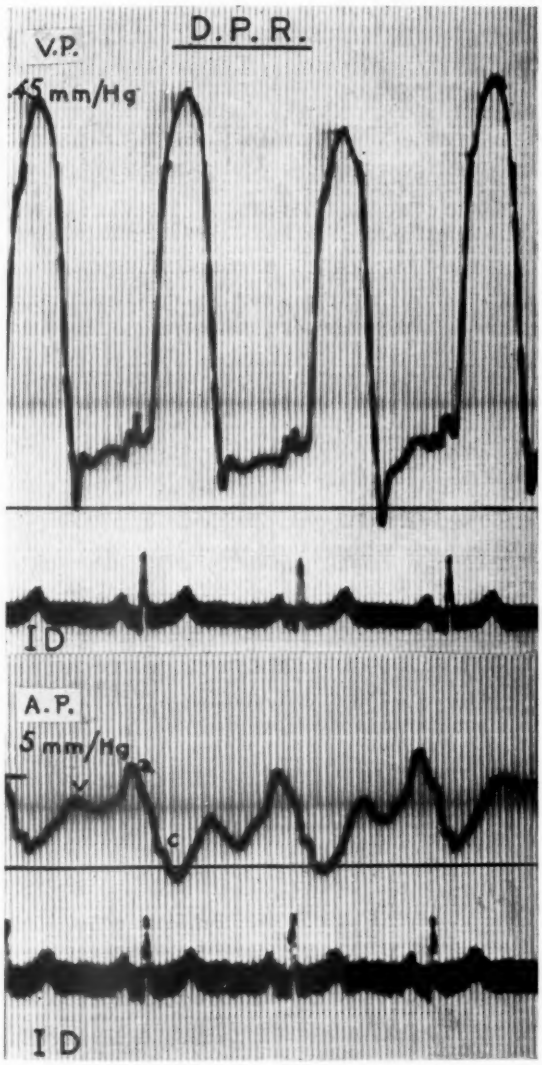


Fig. 3. Normal tracing of right auricular pressure (speed 25 mm/sec).

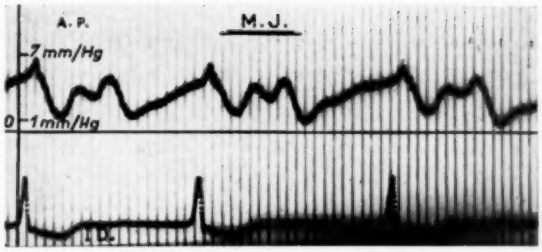


Fig. 4. Normal tracing of right auricular pressure (speed 75 mm/sec).

Tricuspid Stenosis

Of 71 cases of rheumatic valvular heart disease studied at autopsy in our department during the last four years, 16 presented tricuspid stenosis, either pure or accompanied by insufficiency. This percentage (22.5 per cent) is smaller than that reported in other statistical studies[34] where organic tricuspid disease has been found at autopsy in about one-third of cases of chronic rheumatic heart disease. Clinical symptoms to determine the diagnosis are lacking in the majority of cases. Catheterization has proved to be of real value in establishing the hemodynamic diagnosis of tricuspid insufficiency.

Increased Diastolic A-V Gradient: The criterion which decides the hemodynamic diagnosis is the increase in the diastolic auriculoventricular gradient, consequent to elevation of right atrial pressure. We calculate either the mean gradient between the atrial and ventricular waves during the whole diastole, or only the telediastolic gradient. If, however, only the gradient at the beginning of diastole is taken into account, errors in diagnosis may arise.

Opinions as to the hemodynamic criterion for the diagnosis of stenosis of the valve are not unanimous. Ferrer *et al.*,[11] in two cases which they reported, took into account the gradient at the beginning of diastole of the right ventricle. McCord *et al.*[28,29] observed that in only one of three cases which presented stenosis the diagnosis was confirmed surgically. They consider

that it is the gradient at the beginning of diastole which characterizes tricuspid stenosis. Gibson and Wood,[13] in their study of 12 cases, used the highest gradient during the course of diastole to establish the diagnosis of tricuspid stenosis. Killip and Lukas[20] have observed a gradient of 3 to 4 mm Hg during diastole, and autopsy has nevertheless shown that no tricuspid stenosis existed.

The highest diastolic gradient we observed in our cases is 23 mm Hg. To show the degree of difference in the gradient, we present the curves of three cases: two showing sinus rhythm, the other showing atrial fibrillation. These are two cases of organic tricuspid disease with predominant stenosis and one case of pure stenosis. The diastolic gradient in Figure 5 is 14 mm Hg; the gradient in Figure 6 is 12 mm; and in Figure 7 it is 4 mm. It will be seen clearly in the first two cases that the stenosis is accompanied by insufficiency: the atrial curve presents a

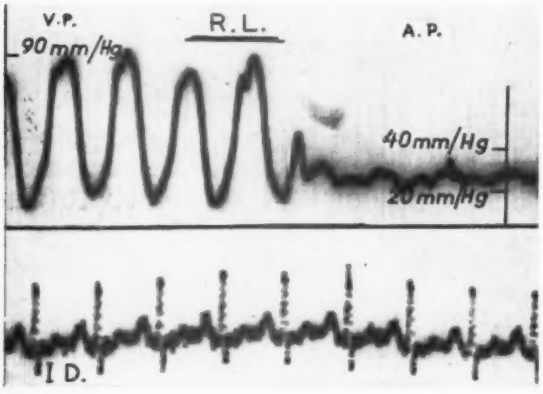


Fig. 5. Right auriculoventricular tracings of tricuspid stenosis, diastolic gradient 14 mm Hg.

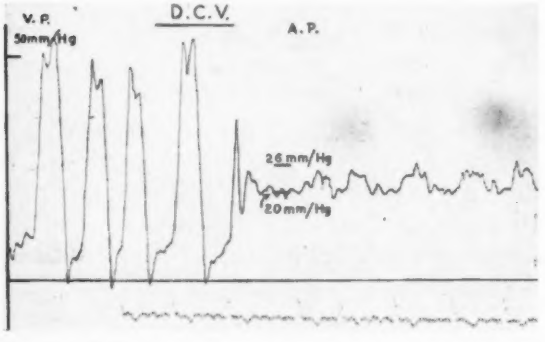


Fig. 6. Right auriculoventricular tracings of tricuspid stenosis, diastolic gradient 12 mm Hg.

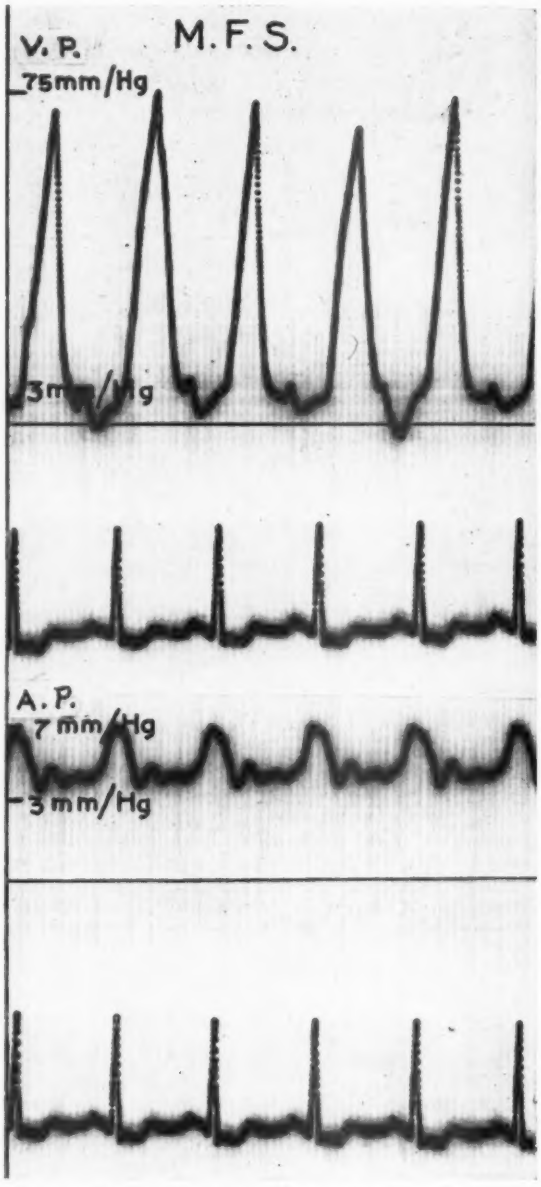


Fig. 7. Right auriculoventricular tracings of tricuspid stenosis, presystolic gradient 4 mm Hg.

systolic plateau. Exertion accentuates the diastolic gradient of tricuspid stenosis.

Combined Stenosis and Insufficiency: The experience we have gained from our research enables us to confirm the observations of others[11,14,18,19,29,36] that stenosis is almost always accompanied by insufficiency. It is necessary to take this fact fully into account when considering the surgical treatment of tricuspid stenosis. On the one hand there is the difficulty in selecting patients;

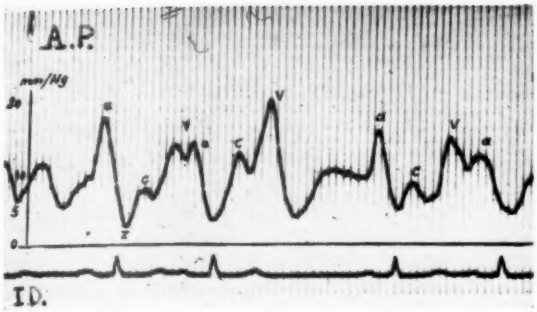


Fig. 8. Tracing of auricular pressure in tricuspid insufficiency with sinus rhythm.

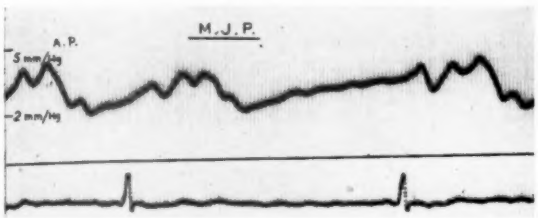


Fig. 9. Tracing of auricular pressure in tricuspid insufficiency with flutter, showing undulations corresponding to the auricular contractions.

on the other there is the risk that commissurotomy may aggravate the insufficiency. We believe that only dye-dilution curves[21,31] are capable of resolving the problem of at least some, if not all, cases of tricuspid disease by permitting us to conclude whether the predominant lesion is stenosis or insufficiency. We are beginning to use this method for this purpose.

Rare cases have been cited where the hemodynamic diagnosis of tricuspid stenosis was not confirmed by surgical intervention. On the other hand, long-established tricuspid endocarditis can exist without hemodynamic alterations. We had one very curious case: Clinically, there were mitral and aortic disease and tricuspid insufficiency; the atrial curve had not shown a significant A-V diastolic gradient and the descent of *x* was normal. On autopsy we found "old lesions of endocarditis of mitral, aortic, and tricuspid valves, with severe stenosis and insufficiency." The aortic insufficiency perhaps masked the hemodynamic picture of tricuspid involvement.

Tricuspid Insufficiency

The physiologic examination of our 620 mitral patients who were catheterized indicated an incidence of 20 per cent with tricuspid insufficiency. In our material we observed different degrees of insufficiency of this valve: insufficiency of a functional nature, insufficiency of an organic nature, and transitory insufficiencies. Those of a functional nature are due to hypertrophy and enlargement of the right ventricle or to an increase in mean atrial pressure. Korner and Shillingford[22] have shown that a close relation exists between mean pressure of the auricle and the appearance of functional tricuspid insufficiency. Once this insufficiency has shown itself, if regurgitation is great, by so much greater will be the enlargement of the auricle and the increase in mean pressure.

Differentiation of Functional and Organic Insufficiency: Organic insufficiency, whether or not

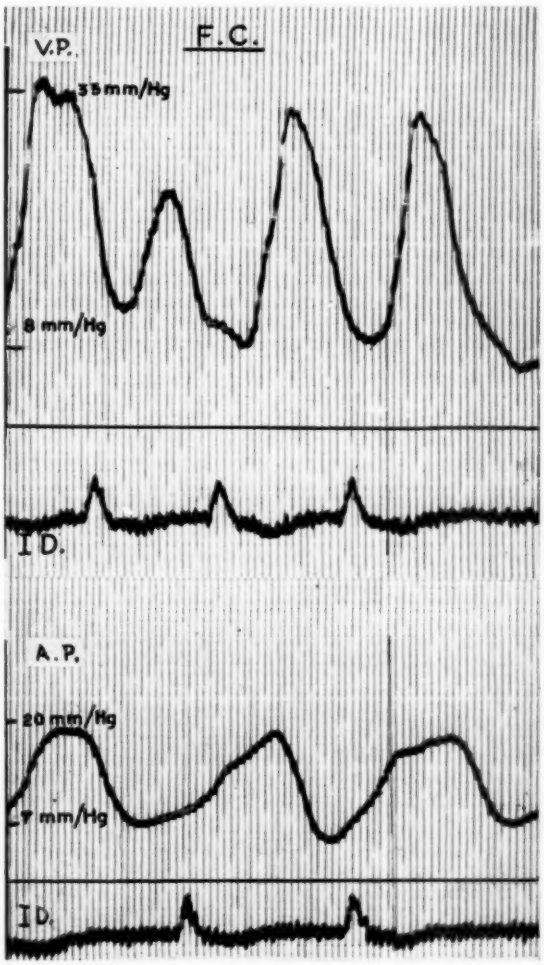


Fig. 10. Auricular pressure tracing of organic tricuspid insufficiency.

accompanied by stenosis, is due to rheumatic valve disease. The early and accentuated elevation of V and the accentuation of the diastolic collapse are, from the hemodynamic point of view, the fundamental characteristics of insufficiency. We have been able to establish that a wave of early systolic regurgitation, with or without a little plateau, usually corresponds to functional insufficiency; more prolonged waves of systolic regurgitation and a more extended plateau are characteristic of organic insufficiency. The shape and the amplitude of the tracings therefore are variable and enable us to appreciate the degree and nature of tricuspid insufficiency. In certain cases of tricuspid insufficiency, with normal sinus rhythm or with atrial fibrillation, there is a lowering of *x* corresponding to the descent of the base, but the lowering of *y* is more accentuated. The curve resembles that of constrictive pericarditis, where there is no reason to suspect systolic regurgitation. In Figure 8 we observe the curve in a case of tricuspid insufficiency with normal sinus rhythm. The regurgitation wave with deep *y* follows immediately after isometric contraction.

Effect of Atrial Flutter and Fibrillation: Figure 8 shows the influence of extrasystoles on the regurgitation wave which is increased during the compensatory pause. In atrial flutter the tracings present undulations corresponding to the atrial contractions (Fig. 9); we observe the beginning of isometric contraction (*C*) very clearly and the regurgitation wave which occupies the whole of systole. The descent of *x* may be more marked, but it is always less than *y*. The regurgitation wave in cases of marked or-

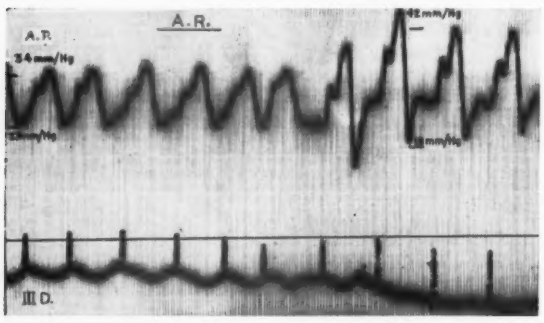


Fig. 11. Auricular pressure tracing of organic tricuspid insufficiency, showing increased regurgitation wave after deep breathing.

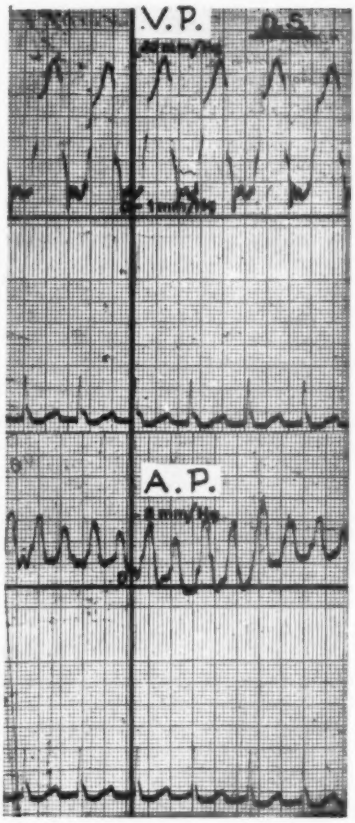


Fig. 12. Tracing of auricular pressure during paroxysmal supraventricular tachycardia provoked by catheterization.

ganic tricuspid insufficiency, where the atrium is so to speak "ventricularized" (Fig. 10), constitutes by itself the atrial curve. The curve of Figure 11 is also of ventricularization but the beginning of ventricular isometric contraction is clearly marked. The C wave is more evident after deep breathing and the regurgitation wave increases.

Comparison of Tricuspid and Mitral Insufficiency: When we compare the curves of tricuspid insufficiency with those of mitral insufficiency we see that they are similar in spite of the different behavior of everything upstream from the auricles and the different structure of each valvular apparatus. In one-third of our cases of tricuspid insufficiency clinical examination either gave only a slight suggestion of its presence or none at all. But does the curve make diagnosis always possible? There are cases of doubtful interpretation. When we try to compare the right and left tracings of valvular insufficiency

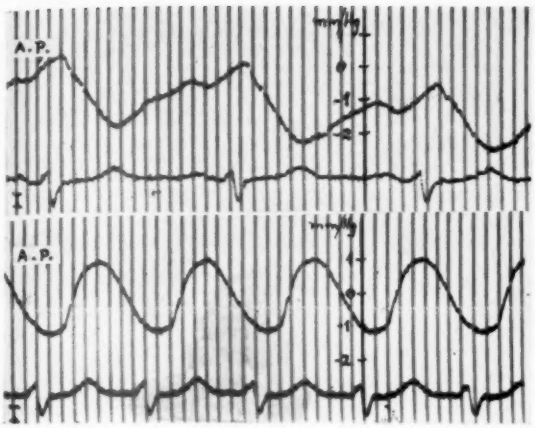


Fig. 13. A single wave occupying systole and diastole during a crisis of supraventricular tachycardia provoked by catheterization. *Upper curve*, normal sinus rhythm. *Lower curve*, paroxysmal supraventricular tachycardia.

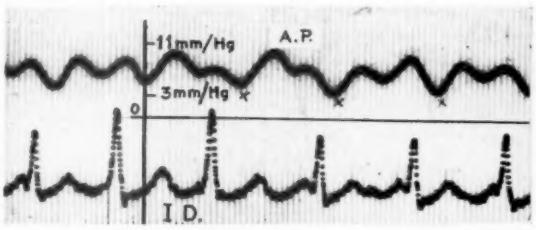


Fig. 14. Tracing of auricular pressure in paroxysmal flutter during catheterization with *x* descent more marked than *y* descent.

we note in the curves considered to be typical the resemblance to which we have just referred.

Curves registered during operations and by bronchoauricular puncture include some with a large V wave similar to the regurgitation wave which occupies the whole systole[1,9]; the operation however, showed that no regurgitation existed. For the differential diagnosis of mitral insufficiency, Allison and Linden[1] proposed the following method: They compared the values of the pressure of the left atrium at the beginning and the end of contraction of the ventricle, that is to say at point *z* and point V. If the mitral valve does not close completely then there is an important systolic regurgitation which raises V and increases the difference (Pv − Pz). This can better be expressed as a percentage of the value of V according to the expression Pv − Pz/Pv × 100. This provides us with a number which is called the left auricular mitral value. When we applied the method of Allison and Linden to the right atrium in the differential diagnosis of tricuspid insufficiency, we did not obtain the same results as those obtained by them for mitral insufficiency. The doubt lies above all in the alteration of *x* in cases of atrial fibrillation.

The Relation Between Atrial Fibrillation and Tricuspid Insufficiency: According to the conclusions of the studies of Little,[25] atrial systole creates an elevation of pressure which is transmitted to the ventricle with a certain delay. When the pressure reaches its maximum in the right ventricle, the auricle is already in a position of "relaxation;" the gradient of pressure which has been created facilitates the occlusion of the tricuspid valve immediately before the ventricular systole. Little[24] states that when ventricular contraction is not preceded by sufficient atrial contraction, the cusps oscillate at the beginning of systole and are late in closing. This delay in

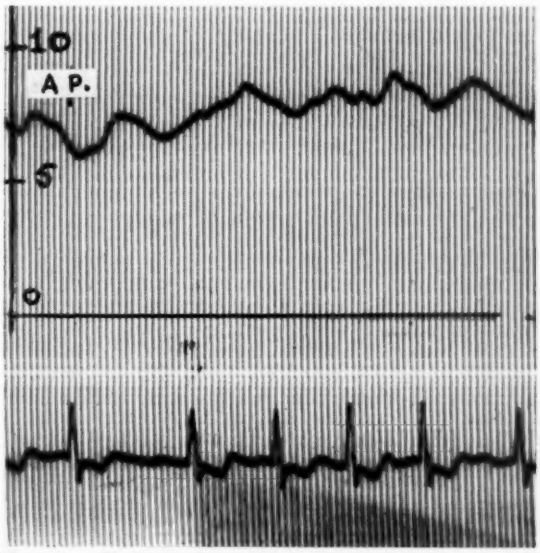


Fig. 15. Tracing of auricular pressure in atrial fibrillation during catheterization with *x* descent more marked than *y* descent.

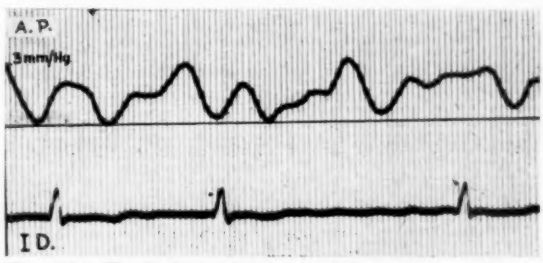


Fig. 16. Typical tracing of atrial pressure pulse in auricular fibrillation due to arteriosclerotic heart disease.

closure of the valve causes a small regurgitation. Several authors[3,16] maintain that atrial fibrillation plays an important role in the formation and aggravation of tricuspid insufficiency. They show that tricuspid insufficiency appears rarely in their cases of auricular flutter, but on the other hand, almost always in their cases of atrial fibrillation.[16] They therefore suggest that this arrhythmia may have a hemodynamic connection with valvular insufficiency.

The first argument against this conclusion is the parallelism which ought to exist in the relationship between atrial fibrillation and mitral insufficiency in cases of mitral valve disease. Even if the valves are thickened, the relationship would be the same. In that case insufficiency would be as frequent, or almost as frequent, as stenosis in mitral disease with fibrillation. Digital exploration of the mitral valve before commissurotomy would permit us to appreciate this. Thus, of all our patients subjected to mitral commissurotomy, 16 per cent were suffering from pure stenosis and atrial fibrillation. In none of these cases did the surgeon find any sign of mitral regurgitation. Why would not the same phenomenon be produced here, in spite of the different anatomic conditions of the two valves? It seems to us important in resolving this problem to observe the atrial curves during paroxysmal flutter and fibrillation provoked in the course of cardiac catheterization, and during fibrillation in arteriosclerotic heart disease.

Paroxysmal Atrial Flutter and Fibrillation Provoked by Catheterization in Patients Without Tricuspid Insufficiency: During catheterization, the atrial pressure pulse in paroxysmal supraventricular tachycardia may present the shape shown in Figure 12. Sometimes a single wave occupying systole and diastole may appear as shown in Figure 13. In this case fluoroscopy seemed to show that contraction of the auricle and ventricle were simultaneous.

After the appearance of atrial flutter and fibrillation provoked by catheterization we noted no connection between the mechanical and the electrical phenomena. The pulse tracings show the *x* descent to be more marked than the *y* descent (Figs. 14 and 15). We have also observed paroxysmal fibrillation provoked by catheterization in which the tricuspid valve became insufficient. These were cases of patients suffering from myocardial insufficiency and presenting an enlarged right auricle. This insufficiency of the myocardium seems to us to be essential in the mechanism of tricuspid insufficiency when this coincides with atrial fibrillation.

Atrial Fibrillation in Arteriosclerotic Heart Disease: Figure 16 shows a typical curve of atrial pressure pulse in this condition. It does not show the findings of tricuspid insufficiency. However, in many cases of atrial fibrillation there is no *x* descent—exactly as in tracings of left atrial pressure in patients suffering from atrial fibrillation—even when we are quite sure that there is no mitral insufficiency (absence of regurgitation). Since the majority of cases of functional tricuspid insufficiency present atrial fibrillation, the disappearance of *x* (descent of base) is not a diagnostic proof of insufficiency, in spite of the generally accepted connection between tricuspid insufficiency and atrial fibrillation. In the latter, the auricle has neither systole nor diastole. Its physiology changes; it does not behave in the same way as the auricle without fibrillation in relation to ventricular systole; and the *x* descent is not as apparent as in normal rhythm. Nevertheless, the descent of the base is observed in certain cases of atrial fibrillation, where the atrial pressure is not too high. When it is very high it produces a small systolic regurgitation, especially following a longer diastolic interval. We will show later the results of experimental atrial fibrillation.

TABLE I

Relation Between Tricuspid Valve Disease and Pulmonary Arterial Hypertension

Group	No. of cases	Tricuspid insufficiency		Tricuspid stenosis or tricuspid disease	
		No.	%	No.	%
I	90	2	2.2	—	—
II	167	22	13.0	2	1.2
III	76	14	18.5	2	2.6
IV	80	20	25.0	1	1.2
TOTAL	413	58	14.0	5	1.2

Pulmonary Hypertension in Tricuspid Disease

In a previously reported[6] series of 413 cases of rheumatic mitral heart disease, only 71 cases (17.2 per cent) had tricuspid insufficiency or tricuspid disease diagnosed by catheterization, and of these only 16 presented clinical symptoms of tricuspid insufficiency or stenosis. In the others the diagnosis of tricuspid disease was made only by hemodynamic examination. We have classified the 413 cases arbitrarily into four groups, according to the systolic pressure in the pulmonary artery:

Group I. Systolic pressure less than 30 mm Hg (normal), 90 patients

Group II. Systolic pressure between 30 and 49 mm Hg (moderately high), 167 patients

Group III. Systolic pressure between 50 and 69 mm Hg (high), 76 patients

Group IV. Systolic pressure above 70 mm Hg (very high), 80 patients.

Relation of Pulmonary Pressure, Tricuspid Involvement, and Height of Regurgitation Wave: In 63 patients with tricuspid valve involvement in whom we were able to measure the pressure in the pulmonary artery (in the remaining 8 cases we were unable to reach the pulmonary artery) we found values ranging from 24/12 to 125/50 mm Hg. Table I shows that tricuspid insufficiency predominated in groups III (18.5 per cent) and IV (25 per cent). Tricuspid stenosis was found to predominate in group III (2.6 per cent).

These patients are submitted to such high pressures in the pulmonary artery and right ventricle that the systolic regurgitation wave becomes higher unless there already exist certain alterations in the atrial-caval system, provoking a delay or prolonging the systolic regurgitation wave.

The height of the regurgitation wave is not proportional to the systolic jet. It depends rather on the distensibility or rigidity of the atrium and on the quantity of blood it contains. If the atrium and the venae cavae are very distended or if they contain little blood, a large regurgitation may not increase the pressure at all or may increase it only slightly; if the atrium is full or if it is rigid, a small regurgitation may increase considerably the atrial pressure.

TABLE II

Relation Between Degree of Regurgitation and Four Groups of Pulmonary Artery Pressure

Pulmonary artery pressure group	Large regurgitation wave	Small regurgitation wave
I	0	3
II	8	15
III	7	10
IV	11	11
Total	26	39

The systolic regurgitation wave was small in 39 cases and great in 26 cases. If we subdivide each of these groups into the four groups of pulmonary pressure we see, as shown in Table II, that there is no parallelism between the degree of pulmonary hypertension and the size of the regurgitation wave.

Relation of Tricuspid Involvement and Pulmonary Complications: How should we interpret the very slow clinical evolution of rheumatic disease of the tricuspid valve, behaving more or less like chronic constrictive pericarditis? Tricuspid disease has been considered to be one of the causes of the diminution of the pulmonary phenomena of mitral stenosis. We know that even in the absence of tricuspid disease, once insufficiency of the right heart is established, the tendency toward pulmonary complications—stasis and pulmonary edema—diminishes. The cardiac output is also diminished. In both cases the great enlargement of the right auricle and venae cavae seems to protect, if only partially, the pulmonary circulation.

It is believed that pulmonary hypertension and its physiologic manifestations have little repercussion on the evolution of organic disease of the tricuspid valve. This is an erroneous opinion when the organic disease is associated, as it generally is, with mitral valve disease which causes well-known pulmonary disturbances. Reale *et al.*[33] have shown that tricuspid stenosis does not preserve the patients from these alterations; some of the latter, such as dyspnea on exertion, are very marked. Although tricuspid disease does not provoke alterations of pulmonary wedged pressure, it is necessary to recognize that over the general clinical picture of tricuspid

disease the influence of mitral disease weighs heavily.

We have observed pulmonary stasis in 25 patients with tricuspid disease, of whom 8 showed crises of acute pulmonary edema. The pulmonary artery pressures of these patients, with three exceptions (1 in group I and 2 in group II), were very high. In one patient suffering from tricuspid stenosis and insufficiency with very severe clinical symptoms, the pulmonary artery pressure was 75/40 mm Hg (55 mm average), and the pulmonary capillary pressure was 45/25 mm Hg (35 mm average); however, he showed no tendency to develop acute pulmonary edema. Of the 8 patients suffering from acute pulmonary edema, 1 had sinus rhythm, 6 had flutter-fibrillation and 1 had paroxysmal fibrillation. Mitral valvulotomy was carried out in 3 of the 8 cases. The pulmonary artery pressures were, respectively, 75/40 (mean 52), 70/30 (38), and 32/18 (25) mm Hg. Biopsy of the lung showed only septal fibrosis in the first case and swelling of the internal layer of the small arteries in the other two; these alterations are the same as those presented by other patients who had never had acute pulmonary edema.

During the course of the development of tricuspid disease the pulmonary artery pressure sometimes decreases and sometimes increases slightly. In one patient suffering from tricuspid disease with severe cardiac congestive insufficiency, catheterization repeated one year later showed a decrease in the pulmonary artery pressure from 45/12 (32) to 33/12 (22) mm Hg. In another patient the second catheterization repeated four years after the first showed a slight increase in the pulmonary artery pressure, from 41 to 45 mm Hg (average).

TABLE III

Relation Between the A-V Diastolic Pressure Gradient of Tricuspid Stenosis and Pulmonary Artery Pressure

Case	A-V diastolic gradient (mm Hg)	Pulmonary artery pressure (mm Hg)
1	23	60/20
2	17	45/25
3	12	90/50
4	10	50/30
5	6	73/47

Relation of Severity of Tricuspid Stenosis and Pulmonary Artery Pressure: According to Yu *et al.*[38] and McCord *et al.*,[28,29] pulmonary hypertension varies inversely with the intensity of tricuspid stenosis in patients suffering simultaneously from mitral stenosis and tricuspid stenosis. If we compare the A-V gradients of diastolic pressure in five of our cases (Table III) we see that such an exact correlation does not exist. Al-

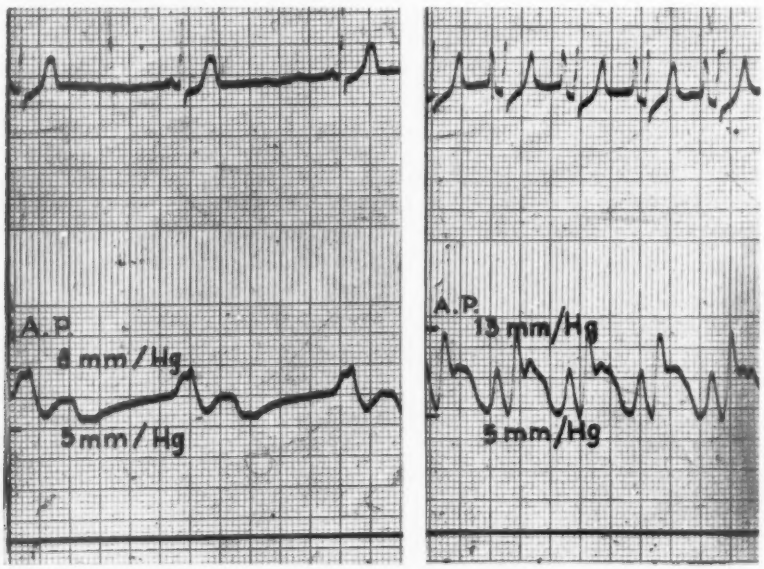


Fig. 17. Auricular pressure in dog. *Left*, normal curve. *Right*, experimental tricuspid insufficiency.

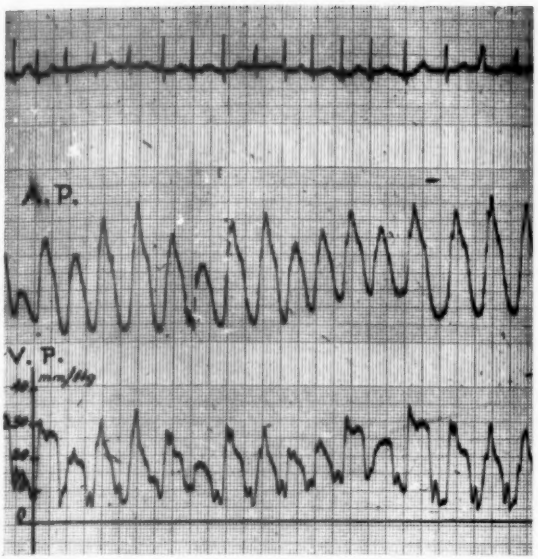


Fig. 18. Tracing of auricular pressure in experimental tricuspid insufficiency, ventricularized after provoking auricular fibrillation.

though the smallest pulmonary artery pressure in this series does not correspond to the highest gradient, it is a fairly high gradient (case 2). Moreover, although a high pressure (73/47) does correspond to the lowest gradient (6 mm, case 5), the patient who has double this gradient (12 mm) has a still higher pulmonary artery pressure (90/50 mm, case 3).

Experimental Tricuspid Insufficiency and Tricuspid Valve Function During Arrhythmias

We have extended our studies to experimental tricuspid insufficiency and its relation to atrial fibrillation and pulmonary hypertension. In our hemodynamic laboratory my collaborators, A. Oliveira, Sousa Borges, and J. Maltez, and I have studied experimental tricuspid insufficiency in 50 dogs.

METHOD

The experiments were carried out in dogs with weights varying between 8 and 13 kg. They were anesthetized with a dose of 30 mg/kg of body weight of a 6 per cent solution of pentobarbital; one hour before this we gave them a subcutaneous injection of 1 per cent chloride of morphine and 0.5 per cent atropine, 1 cc/kg.

Before the surgical intervention we recorded the electrocardiogram, the phonocardiogram at the apex, and sphygmogram, and performed catheterization in the external jugular vein, right cardiac cavities, and pulmonary artery to register the pressures. We then made a large opening in the thorax at the right third and fourth intercostal spaces, with or without resection of the fourth or fifth rib.

In a series of experiments, atrial fibrillation was provoked by the local application of a few drops of Mecholyl. We registered simultaneously the pressures in the right auricle, right ventricle, and pulmonary artery. In another series of experiments, or with the same dogs after the atrial fibrillation ceased, we produced tricuspid insufficiency with a special scalpel introduced through the right auricular appendage, with which we cut either the valve, the chordae tendinae, or both. In this way we produced tricuspid insufficiency of different degrees—small, average, and great. Then we registered the pressures and the electrocardiogram simultaneously. We again provoked atrial fibrillation in the dogs now suffering from tricuspid insufficiency and repeated the registrations.

The dogs did not survive the hemodynamic alterations produced by the great tricuspid insufficiencies. Finally, we examined the heart anatomically. We used the Sanborn manometer for registering the pressures and the Sanborn Polyviso for recording the electrocardiogram.

We have also studied the modifications in atrial pressures and their relation with ventricular systole during ventricular extrasystoles, ventricular tachycardia, bundle branch block, and nodal rhythms provoked during the operative intervention on the valve.

RESULTS

Experimental Tricuspid Insufficiency: In the normal dog, we have noted well-marked A, C, and V waves, although there are many variations. The A wave may be considerably increased, may have the same elevation as the V wave, or may be lower than the C wave. When tricuspid insufficiency is produced a thrill is immediately felt, resulting from systolic regurgitation. The atrial pressure increases immediately and the curve presents different aspects corresponding to the intensity of the regurgitation. We have noted during sinus rhythm a high systolic wave which occupies the entire systole, climbing rapidly and descending more slowly, without a descent of the base (x); or a systolic wave of ventricular form with well marked A and C waves; or again, a high A wave with descent of x and a wave of systolic regurgitation higher than A, climbing rapidly and remaining high during the whole duration of systole (Fig. 17).

When atrial fibrillation is provoked by Mecholyl in a heart presenting tricuspid insuffi-

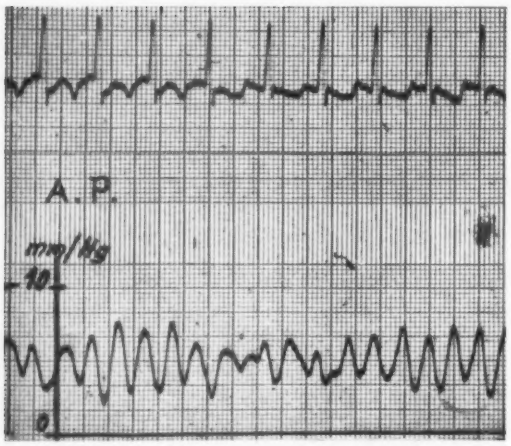
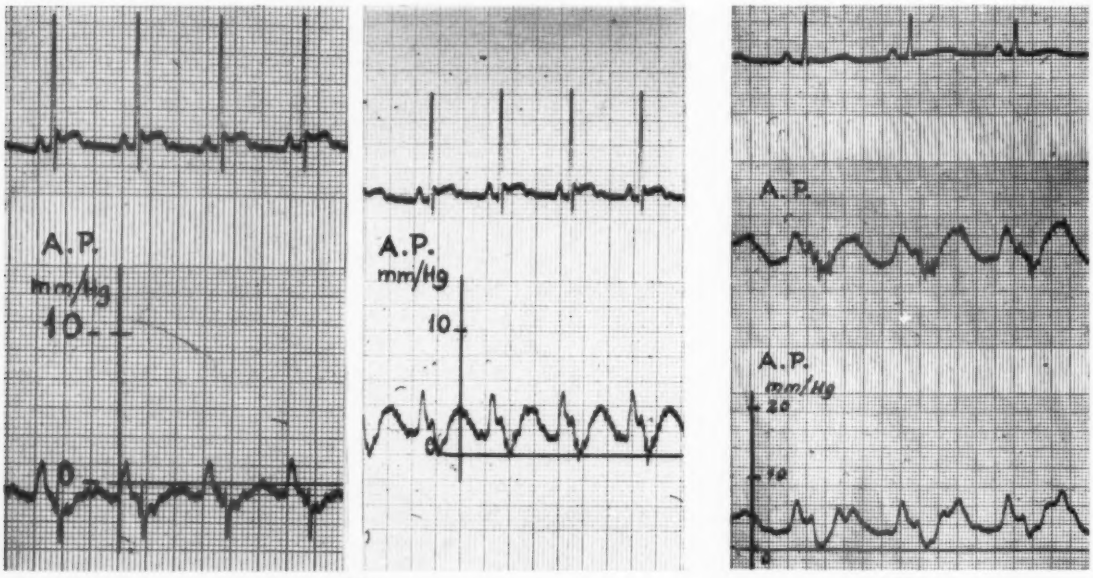


Fig. 19. Tracing of auricular pressure during experimental auricular fibrillation, showing the *x* descent.

ciency the curve of atrial pressure appears to be more intensely "ventricularized" (Fig. 18).

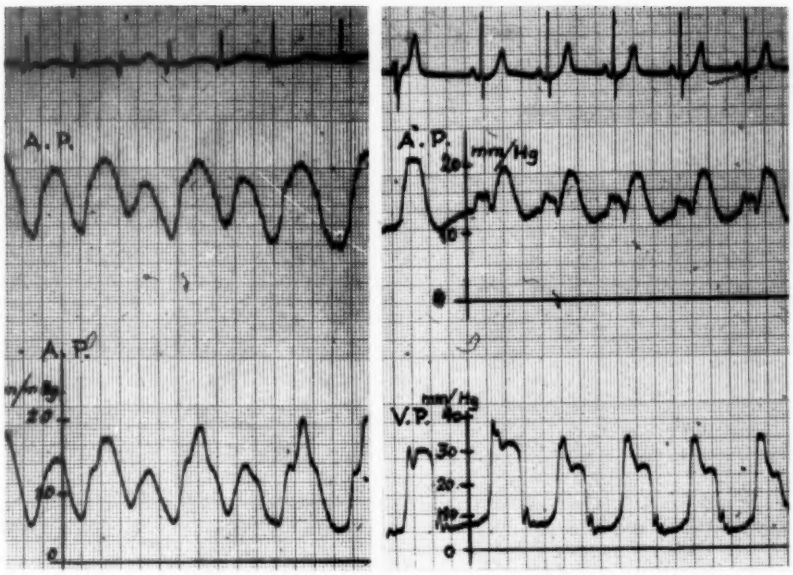
Experimental Atrial Fibrillation Provoked in the Normal Heart: The most frequent aspects presented by the atrial curves are that the curve consists of waves with shapes similar to each other, coinciding or not with the systole. If sometimes we observe an increase immediately after isometric contraction, we can also note a descent of the base (Fig. 19). In these cases the contraction of the auricle is abnormal without systole and without diastole. As we have said already with regard to clinical atrial fibrillation, the pressure curves do not behave like those of a normal atrium. The cusps sometimes close completely but in other cardiac cycles do not close perfectly because of the irregular contraction of the auricle and because their position is not always the same at the beginning of ventricular systole. As a result there is a leak in some of the cardiac cycles.

Experimental Tricuspid Insufficiency and Atrial Fibrillation: We have noted in some experimental cases that the tricuspid insufficiency, in spite of the thrill produced, did not have the hemodynamic repercussions to be expected, but we then provoked atrial fibrillation by means of Mecholyl and the tricuspid insufficiency then showed itself hemodynamically. The influence of the abnormal atrial contraction on the tricuspid valve becomes more striking. The tracings of one of these experiments show these alterations (Fig. 20). As soon as the tricuspid insufficiency commences, the A and V waves are increased but the latter is not so high. The descent of the base (*x*) is deeper than *y*. The alteration of the electric potentials modifies the



20 21

Fig. 20. Experimental tricuspid insufficiency in which the tracings of auricular pressure do not present the typical alterations. *Left*, normal curve. *Right*, after experimental tricuspid insufficiency.
Fig. 21. Tracing recorded some minutes after Fig. 20, in which the V wave reaches the height of the A wave.



22 23

Fig. 22. Tracing recorded a few minutes after Fig. 21, after auricular fibrillation has been provoked by Mecholyl.
Fig. 23. Tracing recorded a few minutes after Fig. 22, after fibrillation has disappeared. The *x* descent is smaller than *y* descent, the V wave is high.

curve. A few minutes later the V wave reaches the limits of A (Fig. 21). Then when we have administered a few drops of Mecholyl, provoking atrial fibrillation, the atrial curve presents the aspect described above in which a single wave almost always occupies the entire systole and diastole, while the isometric contraction corresponds sometimes to a rise, sometimes to a fall in the curve. We again note that the cusps do not close perfectly during certain ventricular contractions. They oscillate and allow an escape of blood into the auricle. A few minutes later there occurs clearly with the atrial fibrillation a ventricularization of the atrium shown by the form of the S wave of systolic regurgitation (Fig. 22). This fibrillation then disappears. The descent of the base (*x*) is much smaller than *y*. The V wave is very high (Fig. 23).

Ventricular Extrasystoles and Tricuspid Insufficiency: The influence of ectopic ventricular systoles is clear in Figure 23. The absence of atrial contraction preceding the ectopic ventricular contraction has provoked a large S wave of regurgitation. A few seconds later the V wave

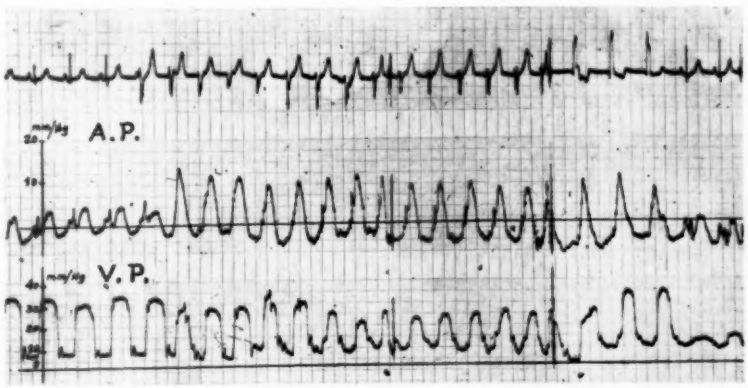


Fig. 24. Alteration in atrial pressure tracing following experimentally provoked alteration of rhythm.

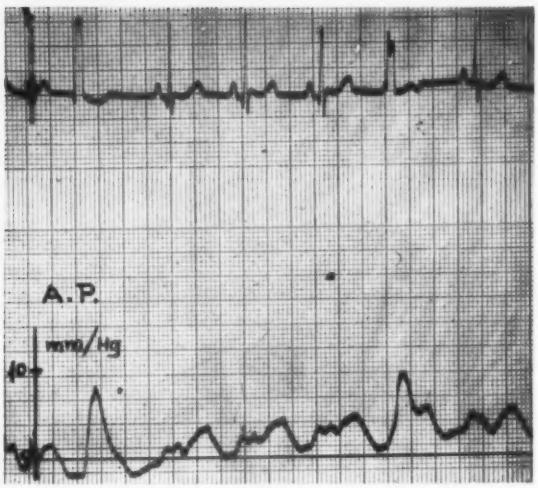


Fig. 25. Alteration in atrial pressure tracing following experimentally provoked ventricular extrasystoles.

is lower, but it presents the shape of a systolic regurgitation wave of organic insufficiency.

The tracing of Figure 24 shows how a change in ventricular rhythm transforms the V wave, which formerly did not exceed the level of the A wave, into a very clearly marked S wave of systolic regurgitation. Two isolated ventricular extrasystoles in the next tracing (Fig. 25) show the influence exercised on the tricuspid valve when there is no atrial contraction.

Our findings are in agreement with the conclusions of Little,[24] who maintains that in ventricular contraction without a preceding auricular systole the valves are raised by a hingelike movement at the beginning of ventricular systole. This delay in closure permits systolic regurgitation into the atrium. Therefore, the cause of regurgitation during ventricular extrasystoles lies in the position of the valve at the beginning of ventricular systole, as has been shown by Henderson and Johnson[17] and Little.[24] The existence of a systolic leak under such circumstances, or in atrial flutter or fibrillation when these succeed a more prolonged diastole, is not, as we have seen, sufficient to affirm the existence of permanent tricuspid insufficiency, since the small regurgitation is not constant in all the cardiac cycles.

We have also observed, as was to be expected, a lowering of systolic and diastolic pulmonary pressure after experimentally provoked tricuspid insufficiency.

Summary

In a great number of cases clinical symptoms fail to give the diagnosis of tricuspid stenosis and insufficiency. The phlebogram can be used with advantage in the differential diagnosis of functional insufficiency and organic insufficiency, but stasis in congestive heart insufficiency may produce waves similar to these of tricuspid insufficiency. The most exact method is to register the auriculoventricular curves by catheterization.

Tricuspid stenosis is almost always accompanied by insufficiency. At autopsy of patients with rheumatic valvular lesions, the percentage of cases with tricuspid stenosis was 22.5 per cent. For the diagnosis of stenosis the recommended criterion is the increase in the A-V gradient of pressure during the entire diastole (caused by increased auricular pressure), or the increase in the telediastolic gradient. The highest gradient observed was 23 mm Hg.

Tricuspid endocarditis can exist without hemodynamic alterations, as occurred in one case of mitral and aortic endocarditis and tricuspid disease in which the stenosis was very severe.

In 620 mitral patients who were catheterized, tricuspid insufficiency was found in 20 per cent. One-third of these did not present clinical symptoms sufficient for diagnosis, and the diagnosis was established by the cardiac catheterization.

The early and marked elevation of the V wave, with or without a small plateau, generally corresponds to functional tricuspid insufficiency. Systolic regurgitation waves, more prolonged and with a more extensive plateau (waves of ventricularization), are characteristic of organic insufficiency. The configuration and amplitude of the tracings make it possible to appreciate the degree and the nature of tricuspid insufficiency as shown in several of the tracings.

The development of auricular fibrillation does not provoke tricuspid insufficiency unless there is myocardial insufficiency. Certain curves of auricular pressure in auricular fibrillation do not present the *x* descent, since the auricle in fibrillation has neither systole or diastole. The shape of these pressure curves is therefore different from that of the sinus normal rhythm. A curve with no descent of *x* should not be interpreted as showing tricuspid insufficiency.

On correlating tricuspid insufficiency with pulmonary hypertension it was found that the greater number of cases were encountered in the groups with the highest hypertension. There was no parallelism between the size of the regurgitation wave and the level of pulmonary pressure. There is likewise no correlation between the A-V gradient of diastolic pressure in tricuspid stenosis and the pulmonary pressure.

The atrial pressure curves of tricuspid insufficiency provoked experimentally in dogs are similar to these of human tricuspid insufficiency. The pressure tracing of the right atrium with experimental auricular fibrillation (provoked by Mecholyl) may present a small *x* descent. In spite of this there may be, in some systoles, an escape of blood to the atrium resulting from the hingelike movement of the cusps, when these do not close completely.

After tricuspid insufficiency has been provoked experimentally, the pressure tracings may not show the characteristic alterations. If we then provoke auricular fibrillation, these alterations appear immediately and continue even after the fibrillation ceases. If we provoke ventricular extrasystoles the auricular pressure tracing is completely modified and there appears a wave similar to the regurgitation wave, occupying the entire systole.

The data observed in experimental tricuspid insufficiency in the dog following alterations in rhythm help us to understand the physiopathology of the tricuspid valve in man.

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Seminar on Ballistocardiography*

Ballistocardiographic Changes During Rheumatic Fever

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IN PATIENTS with acute rheumatic fever the high incidence of suspicion of myocardial involvement has resulted in numerous studies of serial observations of the auscultatory, fluoroscopic, electrocardiographic, and other clinical findings present during the course of the disease.

The diagnosis of frank carditis is readily agreed upon when certain signs are present. It is, however, rather more difficult to establish with the same degree of accuracy the definite absence of carditis. Many authors believe carditis is generally present with acute rheumatic fever. The general agreement on the need for prolonged bed rest as an essential aspect of therapy, and the curtailment of activity during convalescence reflects this conviction. However, present-day diagnostic methods are not sufficiently sensitive to be depended upon for conclusive evidence for the lack of involvement of the myocardium in the high percentage of cases of acute rheumatic fever without frank clinical carditis.

Since the detection of certain changes in preexisting murmurs or the appearance of certain types of new murmurs are among the criteria required to establish the presence of carditis,[1] emphasis on direct auscultation during the course of rheumatic fever has always been foremost. Phonocardiography and newer recording methods, such as the sonvelographic recording of murmurs,[2] have demonstrated the presence of changing murmurs or new murmurs in patients with acute rheumatic fever in whom such murmurs had not been observed by careful direct auscultation. These findings with new technics are thus of significant value in contributing to establish the presence of less evident forms of carditis.

BCG FINDINGS IN CARDITIS

Ballistocardiographic studies of groups of healthy children between the ages of 5 and 15 demonstrated that BCG abnormalities were very rarely present in this age group.[5] This prompted a study to observe the variations of the BCG in children with different stages of rheumatic fever activity.[5] This study confirmed that deviations from the normal direct body acceleration BCG correlated with various stages of rheumatic fever activity.

BCG and Severity of Carditis: When there was gross evidence of carditis with congestive heart failure, the BCG was consistently abnormal. When the diagnosis of carditis was established by criteria other than the presence of congestive heart failure, the correlation was less striking. Variations in the PR interval and changes in murmurs were not consistently reflected in BCG abnormalities. The degree of abnormal-

* This issue contains Part VII of the Seminar on Ballistocardiography (edited by Sidney R. Arbeit, M.D.). A schedule of the articles already published, and of future articles in this seminar, may be found on pp. 101–102 of the January, 1959, issue (Vol. III, No. 1).

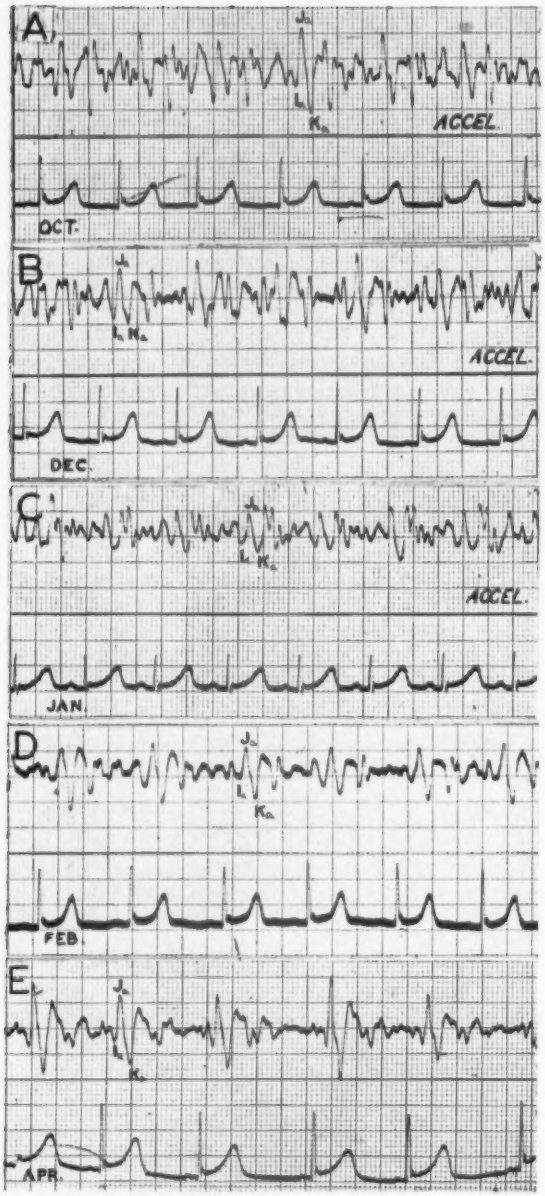

Fig. 1. BCG in acute rheumatic fever with frank carditis followed to recovery. (A) Direct body acceleration tracing taken during the acute stage. The grossly abnormal BCG reflects the abnormal mechanical action of the inflamed myocardium. (B) Acceleration BCG taken two months later. Clinical evidence of carditis has subsided but the BCG is still abnormal. (C) Three months later and the acceleration BCG is beginning to show a repetitive pattern. (D) Fourth month. The acceleration BCG is now repetitive, grade I, but the form of the individual complex is still not normal. Note the round bottom slurred I_a wave. (E) Fifth month. The BCG may now be considered normal.

ity varied also with the clinical status of the patient. Thus, diminution of degree of congestive heart failure or its clinical absence in patients earlier in failure was reflected closely on the BCG. Antirrheumatic therapy when successful in suppressing clinical and laboratory manifestations of rheumatic activity also reverted the BCG pattern to normal or to a less abnormal pattern. In general, variations of the BCG appeared to follow more closely the improved cardiac status of the patient rather than his general improvement.

Duration of BCG Changes: In the group of patients with frank clinical carditis with congestive heart failure, months elapsed before the abnormal BCG returned to normal, despite disappearance of all symptoms of clinical carditis (Fig. 1). This progressive improvement of the BCG lagging behind the clinical improvement of the patient was striking. Those patients in whom the rebound phenomena was noted when therapy was discontinued showed parallel variations of the BCG.

BCG During Convalescence and Recovery Period: Study of the BCG during the first three months of convalescence in a group of 90 patients showed that of 53 patients who had had clinically demonstrable carditis during their acute attack, 53 per cent showed BCG abnormalities, whereas of the 37 patients who had had no demonstrable carditis, only 22 per cent showed BCG abnormalities. Follow-up beyond six months showed that all patients in both groups reverted eventually to a normal BCG except for those with residual extensive rheumatic heart disease. The reversion to normal was more rapid in the group without carditis (Fig. 2). The BCG was repeated on many of these patients beyond one year and was consistently normal. It is noteworthy that even in those cases with persistent valvular deformity and cardiac enlargement, the BCG reverted to normal in the majority of the cases.

Comments

Other authors have studied the behavior of the BCG in patients with definite acute myocarditis. Brown *et al.*[3] concluded that most patients with definite acute rheumatic myocarditis will show some abnormalities in their BCG. Of the seven patients with definite acute rheumatic fever, six had abnormal

BCG's. Mandelbaum *et al.*[4] studied 15 cases recovering from acute rheumatic fever. Serial BCG's in this group showed that except for five patients below 20 years of age, all others showed BCG abnormalities. They studied patients with myocarditis accompanying diverse conditions, concluding that abnormal BCG patterns are more frequent than abnormal electrocardiograms as evidence of myocarditis.

The findings of different authors agree upon the increased frequency of abnormal BCG's associated with certain stages of rheumatic fever. The increased percentage of abnormal BCG's in those patients with clinical carditis correlates even more closely. It is our impression that the BCG is useful in following not only the evident cases of known carditis but all cases of rheumatic fever since, particularly in the age group in which rheumatic fever is more frequent, the percentage of abnormal BCG's in a healthy population of a similar age is extremely low.

Serial tracings in individual cases are helpful in following the acute phase of the disease, the convalescence, and later follow-up. It is our experience that in the vast majority of cases the BCG will return to normal and stay so. The persistence of an abnormal tracing or changes in the same should be further investigated. The appearance of an abnormal BCG at the time of the revisit examinations likewise bears investigating.

It would seem premature to make any further definite statements on the value of the BCG in rheumatic fever at the present time. Additional clinical experience in the use of the BCG in rheumatic fever is definitely indicated.

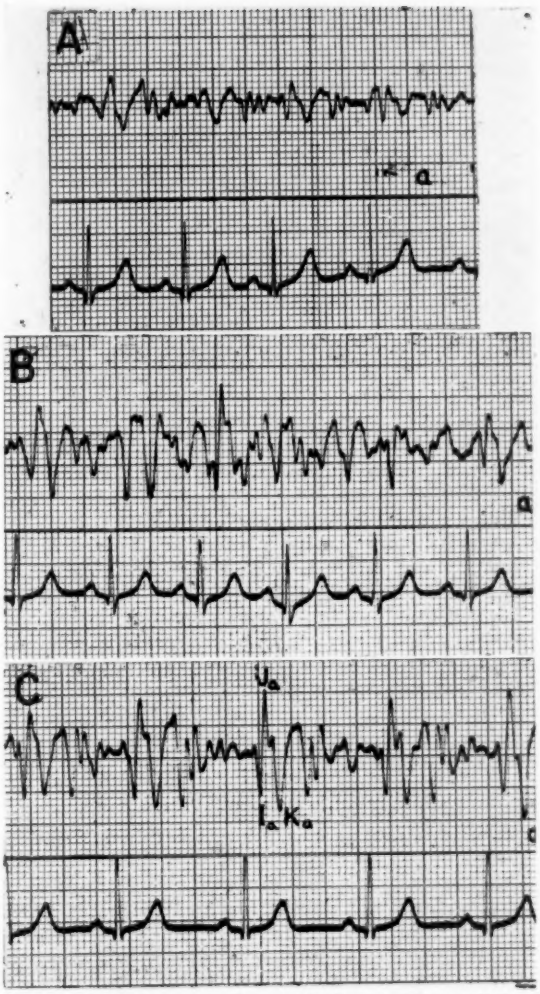

Fig. 2. BCG in acute rheumatic fever without clinical evidence of carditis. (A) Direct body acceleration tracings taken during the acute stage of rheumatic fever are, in a large percentage of cases, severely abnormal such as this one, whether or not other *clinical* evidence of myocardial involvement is present. (B) Acceleration tracing two months later is still abnormal, although the acute stage of rheumatic fever has subsided. (C) Four months later the BCG has reverted to a normal grade O or I, although the form of the individual complex is not normal, reflecting perhaps the residual valvular damage.

Summary

There is a high incidence of abnormal ballistocardiogram in patients with acute rheumatic carditis.

Serial recordings of ballistocardiograms during the course of acute rheumatic fever revealed changes in the BCG correlating with the severity of the acute attack, degree of cardiac involvement, response to therapy, and duration of convalescence.

The low incidence of abnormal BCG's in healthy children suggests that serial BCG's may be valuable in the follow-up of children with acute rheumatic fever.

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The Ballistocardiogram in the Diagnosis of Myocarditis of Nonrheumatic Origin*

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IT IS unusual to find an abnormal ballistocardiogram in a normotensive subject less than 45 years of age. Therefore, when a patient younger than 45 years is found to have an abnormal ballistocardiogram during the course of a systemic disease, it is a reasonable clinical conclusion, providing pre-existing rheumatic heart disease can be ruled out, to assume that the systemic disease has been complicated by a state of myocardial dysfunction. In an older subject, under similar circumstances, it could be argued that the abnormal tracing represents coexistent coronary artery disease. When the recovery of the patient from his systemic disease is accompanied by a ballistocardiogram that has reverted to a normal pattern, it would be strong evidence that a state of reversible myocardial disease had existed. The term "myocarditis" is frequently used to apply to a state of myocardial disease that occurs as part of any systemic inflammatory disease, whether of specific and certain etiology or of uncertain cause. The ballistocardiograph is the most sensitive instrument available to confirm the clinical suspicion that "myocarditis" is present to a degree to be of concern to the doctor.

That the ballistocardiogram could serve as a means for the detection of rheumatic myocarditis was first demonstrated by Dock and the Mandelbaums[1] in 1951. The usefulness of the ballistocardiogram in detecting nonspecific myocarditis was noted at the time by these same authors when two young men with incapacitating weakness following a month of atypical pneumonia, were found to have a markedly abnormal ballistocardiogram. No electrocardiographic changes were found, but ballistocardiographic reversion to normal coincided with clinical recovery in both instances.

CORRELATION OF CLINICAL AND BCG FINDINGS

Infectious Mononucleosis: Because of pathologic reports of high incidence of nonspecific myocarditis in infectious disease,[2] ballistocardiographic studies at rest and after exercise[3] were done on patients recovering from febrile diseases. In most instances the only symptoms suggestive of myocarditis were weakness or slight dyspnea after moderate effort; the majority were asymptomatic. In 23 cases of infectious mononucleosis, nine (39 per cent) showed abnormal traces. Houck[4] states that while autopsy records occasionally may show focal infiltrations of abnormal lymphocytes, a higher incidence of electrocardiographic abnormalities (5 to 50 per cent) is being reported in infectious mononucleosis.[5] Custer and Smith,[6] in their study of postmortem findings in infectious mononucleosis, noted six instances of aggregates of lymphocytes sparsely distributed within the myocardium in small numbers beneath the endocardium. In one patient who died of an accident shortly after recovery from infectious mononucleosis, extensive residual areas of necrosis were found.

Lupus Erythematosus: In 10 cases of disseminated lupus erythematosus, nine showed ballistocardiographic abnormalities. States of clinical remission, induced by adrenal corticosteroid therapy, were usually accompanied by improvement in the ballistocardiogram. The degree of ballistocardiographic reversion toward nor-

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mal appeared to parallel the degree of return of the patients' subjective sense of well-being. Four of the patients with abnormal ballistocardiograms demonstrated electrocardiographic abnormalities.

Scleroderma: Biegelman and his associates[7] studied 15 patients with scleroderma. Eleven had systolic murmurs. Gallop rhythm and multiple arrhythmias were observed, and in six marked cardiomegaly was demonstrated. Five of the patients died; all five showed microscopic evidence of myocardial fibrosis; four showed pericardial thickening; and four showed endocardial and valvular fibrosis. In our four cases of scleroderma, three showed ballistocardiographic abnormality. Electrocardiographic abnormality was found in one case with advanced systemic disease. Adrenal corticosteroid therapy induced striking ballistocardiographic improvement in one case.

Serum Sickness and Allergic Reactions: Ballistocardiographic evidence of myocardial functional impairment was also found in patients with serum sickness (one of two cases) and severe penicillin reaction (two of six cases). The electrocardiograms of all these patients were normal.

Acute Glomerulonephritis: It is interesting to note that in 6 patients with acute diffuse glomerulonephritis (aged 19, 24, 27, 37, 39, and 44), all showed ballistocardiographic abnormalities with the exception of the 19-year-old patient. Peters[8] made the observation that congestive heart failure is a feature of most cases of acute glomerulonephritis. In five instances, the ballistocardiogram ultimately returned to normal, leaving no doubt that myocarditis had been present. There were no electrocardiographic abnormalities in any of these cases. In three cases (aged 18, 28 and 36) with the nephrotic syndrome, normal ballistocardiograms were obtained initially and in follow-up studies.

Trichinosis: Roehm[9] reported a case of trichinosis showing ballistocardiographic evidence of myocarditis. We studied a similar patient who showed marked ballistocardiographic abnormalities. Prednisone was given for three weeks; the ballistocardiogram returned to normal after the fourth week.

Pneumonia: In studies on 15 patients convalescing from pneumonia, ballistocardiographic abnormalities were noted in three of the subjects. In two, the ballistocardiogram returned to normal within seven weeks after the onset of the illness; the third failed to show ballistocardiographic recovery after six months of observation, but was asymptomatic.

Two instances of electrocardiographic confirmation of myocarditis in these cases of pneumonia were found in young patients with persistently normal ballistocardiograms. Dock's[10] concept of presbycardia may account for this unexpected finding. In young people with proved active rheumatic carditis, similar findings have been previously reported.[11] According to Dock, the heart of youth, free of involutional change, is better able to carry on its function in the presence of myocarditis than those over 20 years of age. However, in adolescents where careful serial traces were done, comparative studies of ballistocardiograms taken before and after recovery from severe illness will often show striking quantitative changes.

The ballistocardiographic abnormalities found in our cases of myocarditis were nonspecific. Abnormalities of the I-J stroke configuration were most important. Low amplitude and notching were noted. Prominent H and L waves were usually found to accompany the systolic J wave abnormalities. When simultaneous lateral thoracic ballistocardiograms[11,12] were done, marked prominent diastolic waves were often detected. Prominent diastolic movement in the lateral thoracic record is a markedly abnormal finding in young subjects.[13] With recovery, these diastolic complexes disappear in the head-foot record as well as the lateral thoracic trace; the systolic complexes increase in amplitude and regain normal configuration.

Discussion

In a high proportion of our subjects between 20 and 35 years of age, abnormalities in the ballistocardiogram due to carditis appeared only after the light exercise test.[3] In older subjects exercise seemed to accentuate the abnormalities noted during the resting test.

The cause of the ballistocardiographic abnormalities is to be found in the infiltration of

the myocardial fibers which is detected pathologically. It is reasonable to expect that this infiltration would result in myocardial fiber functional disturbance. Normal myocardial function is the basic requirement for a normal ballistocardiogram. In most instances of myocarditis it may be postulated that the ballistocardiographic abnormalities are related to incomplete systolic ejection, which leads to a rise in left ventricular diastolic pressure, a rise in pulmonary artery pressure, which in turn causes increased resistance to right ventricular ejection. These phenomena may develop only after exercise and represent a state of heart failure.

That congestive heart failure is responsible for the ballistocardiographic changes is suggested by the effectiveness of digitalis in improving the ballistocardiogram. This concept coincides with Peters'[8] observations in acute nephritis. In subclinical failure, with a minimal rise in pulmonary resistance, the ballistocardiogram may show a decrease in the I-J stroke and an increase in respiratory variation. As failure becomes more advanced return flow to the heart is decreased and the rise in venous pressure augments the speed of diastolic filling of the ventricles. The lateral and head-foot ballistocardiograms may both show large H and/or L waves; I is reduced in size and may

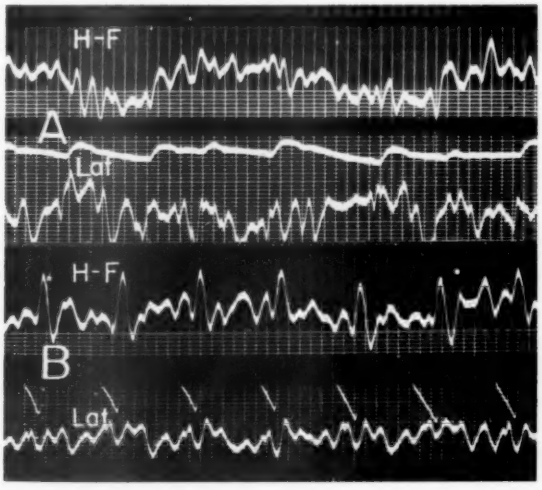

Fig. 1. Case 1. Disseminated lupus erythematosus during acute stage (A) and after treatment with steroids (B). H-F is the classic head-foot BCG obtained with the Dock technic.[11] Lat. is the lateral thoracic BCG.[11,12]

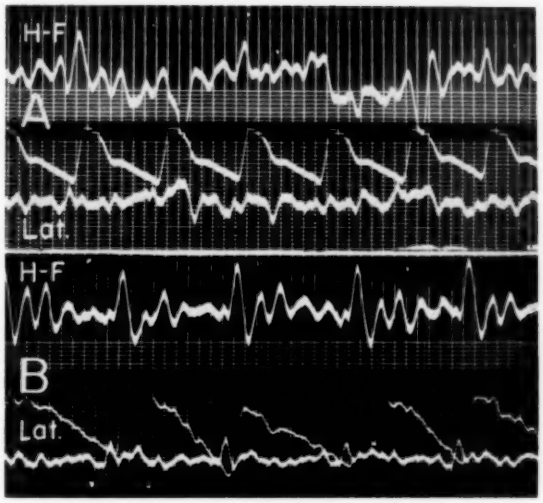

Fig. 2. Case 2. Bronchopneumonia during acute stage (A) and after recovery (B).

be absent so that H-J fuse into a plateau. As the heart dilates and gallop rhythm becomes clinically manifest, the diastolic waves completely dominate the tracing.

Illustrative Cases

Case 1. *Lupus Erythematosus:* J. G., a 43-year-old woman, had mild joint pain for three years and fever for four months. She appeared quite ill, and complained of dyspnea on effort. Physical examination on admission revealed auricular fibrillation with a rapid apical rate and a diastolic gallop. Blood studies confirmed the diagnosis of disseminated lupus erythematosus.

The ballistocardiogram on admission (Fig. 1*A*) demonstrated small amplitude systolic complexes in the head-foot record and, by comparison, large complexes in the lateral thoracic record. An electrocardiogram taken at this time was normal except for auricular fibrillation. After 12 weeks on adrenal corticosteroid therapy, there was a striking clinical improvement. At this time the head-foot ballistocardiogram (Fig. 1*B*) had reverted to normal. In the lateral thoracic ballistocardiogram (Fig. 1*B*) the prominent waves occurred in systole with diastolic activity diminished. The heart rhythm was regular.

Case 2. *Bronchopneumonia:* A 38-year-old auto mechanic ran a 14-day febrile course with

an illness characterized by productive cough and sweats. Chest x-ray revealed a bronchopneumonia. Six days after subsidence of temperature, when ambulation was begun, the patient complained of palpitations and great weakness with activity. Blood pressure in the upright position was normal. The electrocardiogram at this time was normal.

The resting ballistocardiogram (Fig. 2*A*) revealed low amplitude complexes in the head-foot tracing and prominent mid-diastolic waves in the lateral thoracic record. During the next 30 days he gradually regained his strength and returned to work seven weeks after the initial ballistocardiogram. The ballistocardiogram at this time (Fig. 2*B*) showed a normal head-foot tracing and an unremarkable lateral thoracic record.

Case 3. *Penicillin Allergy:* J. W., a 32-year-old electrician, an athlete, received penicillin for a carbuncle of the neck. Ten days later, he developed swollen painful joints, fever, and urticaria. He was treated with antihistaminics with no response. He was seen in consultation one week later. Clinical examination and electrocardiogram were normal.

The resting head-foot ballistocardiogram (Fig. 3*A*) showed grade 1 respiratory variation and tall L waves. After light exercise (Fig. 3*B*), the head-foot ballistocardiogram showed grade 2 respiratory variations with expiratory fused H-J waves. The patient responded well to cortisone, and after ten days was symptom-free. He felt well enough to return to work. Six weeks after the initial study, the resting and exercise head-foot ballistocardiograms were normal (Fig. 3*C* and *D*).

This case illustrates: (1) the importance of light exercise in bringing out abnormalities due to impaired myocardial function; and (2) the changes in the amplitude of the complexes of the recovery trace as compared to the initial study.

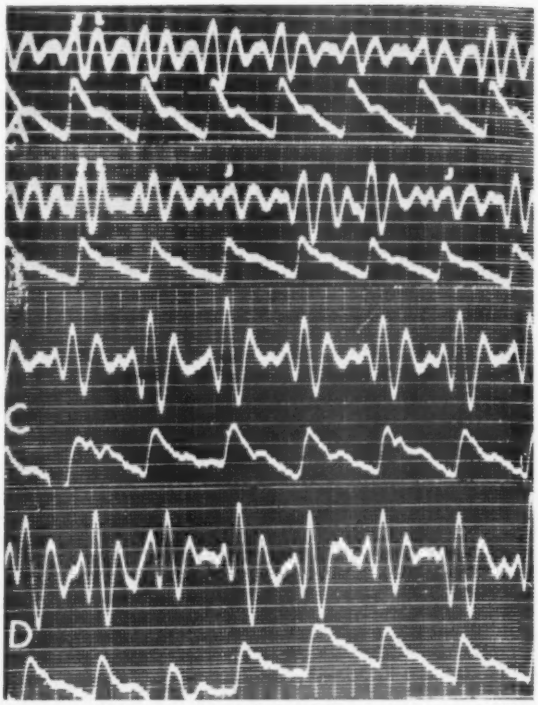

Fig. 3. Case 3. Carditis associated with penicillin sensitivity. A and B are resting and exercise BCG's during acute phase. C and D are resting and exercise records after recovery. All BCG's are classical head-foot tracings.

Summary and Conclusions

While the ballistocardiogram does not furnish a pattern distinctive for myocarditis, ballistocardiographic abnormalities may be the only objective evidence of myocardial disease. In a subject recovering from systemic infection, this abnormality should be respected and lead the clinician to enforce further rest.

Myocarditis in adults is frequently associated with an abnormal ballistocardiogram. In children, the significance of the initial traces may become apparent only after comparison with the recovery ballistocardiogram. In subjects between the ages of 20 and 30, where myocarditis is suspected, the light-exercise test may bring out abnormalities in the ballistocardiogram where the resting trace was normal.

Abnormal ballistocardiograms have been observed in disseminated lupus erythematosus, scleroderma, trichinosis, acute diffuse glomerulonephritis, infectious mononucleosis, pneumonia, serum sickness and drug sensitivity reactions. Recovery of the patient with the reversion of the ballistocardiogram to normal has served as evidence for the correctness of the diagnosis of complicating myocarditis in these illnesses.

It is our experience that during the active stage of myocarditis, abnormal ballistocardio-

graphic patterns are more frequent than electrocardiographic evidence of disease.

Ballistocardiography should be regarded as an important supplement in the observation of patients who are ill with or recovering from collagen diseases, infectious or virus diseases, and acute glomerulonephritis. It serves as a guide in detecting myocarditis and as an index of complete recovery.

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Reports on Therapy

Treatment of Angina Pectoris with Catron (JB516)*

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SEVERAL reports have shown that iproniazid phosphate is beneficial in preventing the pain of angina pectoris.[1–3] However, it has not had widespread usage because of the incidence of severe reactions. Recently we have made some observations on another monoamine oxidase inhibitor, Catron.† Catron (JB516) is a hydrazine analogue of amphetamine. We have used it in over 50 patients with mental depression, essential hypertension, terminal cancer, and coronary artery disease. This report is concerned with the observations in 31 patients with severe angina pectoris.

The patients were selected from a large group and had typical attacks of substernal chest pain and positive electrocardiographic findings on exertion or during spontaneous attacks. All of the cases were extremely clear-cut without any reasonable doubt of diagnosis. These were nonclinic patients receiving individual attention, and as a group were of unusually high intelligence. Most of the patients were receiving therapy consisting of long-acting nitrites, nitroglycerin, weight reduction, low-fat diets, exercise, sedation, and in some instances anticoagulants and radioactive iodine, without satisfactory control at the time Catron was added to their regimen.

RESULTS

We have classified the results as "marked improvement," "moderate improvement," and "no improvement." "Marked improvement," indicating that the patient had no further pain and was able to discontinue the use of nitroglycerin, was observed in 12 patients. "Moderate improvement," indicating that there was notable improvement but the patient was unable to completely discontinue the usage of nitroglycerin, occurred in 11 patients. In 8 patients there was questionable or no improvement.

DISCUSSION

Our data indicate that Catron is a drug of great value in the treatment of serious angina pectoris. However, this is a preliminary report and the limitations of the study are well recognized. Nonetheless, some of the patients have been successfully treated for nine months. In most instances mood elevations and cheerful outlook were encountered. There were no attempts at substitution placebos or double-blind evaluation techniques. Nevertheless, it would appear that Catron is potentially an important drug in the symptomatic treatment of angina pectoris and that further observations and experience are indicated.

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† Lakeside Laboratories, Inc., Milwaukee, Wisconsin.

DOSAGE

The dosages used have ranged from 3 mg given after each meal to 12.5 mg given twice daily. In general, the most satisfactory dose has been 6.25 mg given on arising and repeated at 3 P.M. As with iproniazid, there is a delay of several days before the beneficial effect is obtained. Once a beneficial effect is obtained, the dosage should then be lowered. Quicker and more dramatic relief of pain is obtained with the larger doses of the drug, but there then occurs the problem of unpleasant side effects. The ideal dosage must be determined for each individual case.

MECHANISM OF ACTION

We have no observations upon the mechanism of action by which the relief of pain occurs. It is not known whether the drug has any beneficial effect upon the coronary circulation or the myocardium. There was no significant improvement in the electrocardiogram of any of these patients. It has been suggested that the effectiveness of the monoamine oxidase inhibitors is due to the sparing effect on norepinephrine normally released from sympathetic nerve endings in the heart. One fact appears certain—that in angina pectoris there is a dissociation of the pain-inducing factors and those causing electrocardiographic changes. It is important to remember that these patients obviously continue to have coronary artery disease even though the anginal pain has been symptomatically relieved and they must continue to be treated for the underlying condition.

TOXICITY

The undesirable effects found have been postural hypotension (5 patients), jitteriness (2 patients), drug rash (2 patients), and insomnia (4 patients). The occurrence of postural hypotension did not appear to be related to the presence of hypertension. Most of the cases of hypotension were controlled by temporarily discontinuing therapy and reinstituting it on a lower dosage. We were able to overcome the hypotensive effect in one case by concomitant use of an adrenal steroid preparation. Insomnia can usually be overcome by lowering the dosage. The rash was of an eczematoid type which cleared up immediately on discontinuing the drug. One unusually apprehensive patient complained of depression, but we are not certain of a cause-and-effect relationship of the drug with this peculiar reaction. There have been no serious toxic reactions such as leukopenia or jaundice. There have been no complaints of impotence.

Three patients developed acute myocardial infarction while taking the drug. In each instance there was rapidly increasing angina at rest, and, in retrospect, these would have to be considered cases of preinfarction angina.

SUMMARY

Catron (JB516), a monoamine oxidase inhibitor, appears to be an antianginal agent which has the combined qualities of effectiveness and low toxicity. It is worthy of extensive trial.

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Small Doses of Iproniazid in the Therapy of Angina Pectoris

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IN 1957 and 1958, Cesarman[1] and Cossio,[2] working separately, each reported beneficial effects from the utilization of iproniazid (Marsilid*) in patients suffering from angina pectoris. Each appears to share the same conclusion that the mechanism of action is not one of simple vasodilatation but rather perhaps of direct action on cardiac metabolism. In his article Cesarman describes various side effects of the drug as consisting of vertigo, meteorism, mouth dryness, constipation, dysuria, euphoria, somnolence, or tremors. He regarded the side effects in the cases he studied as being of no particular significance. Cossio noted side effects of faintness, weakness, paresthesia, nervousness, syncope, impotence, and muscular twitchings in this order; only cessation of therapy could abolish them completely.

In the early part of 1958, the medical profession of the United States received circulars warning of the possibility of extremely hepatotoxic effects of iproniazid and cautioning strongly against its indiscriminate use. Attention was also called to the desirability of the utilization of the minimal effective dose. Both Cesarman and Cossio began with 150 mg of the drug given in three divided doses daily, with the suggestion that the dosage be reduced stepwise, possibly achieving a maintenance dose of 25 mg three times a day. It is assumed that this therapy, once embarked upon, would have to be continued more or less permanently, since Cesarman reported that in three to eight days following cessation of the medication, symptoms appeared to return. Cossio recommends not abandoning this regimen as having failed before trying a 50-mg dose four times daily for four to six weeks.

CASE MATERIAL AND RESULTS

The present paper is a compilation of experience with 13 patients with severe to nearly intractable angina satisfactorily controlled on doses of iproniazid of 10 mg daily. For the most part these were patients ranging in age from about 55 to 70 years, males considerably in the majority, and most having suffered a previous myocardial infarction. All were inadequately controlled insofar as subjective symptoms were concerned in that frequent doses of nitroglycerin were required, in one instance often as many as 25 tablets per day, to permit of ordinary, limited physical activity. None clearly suffered from angina decubitus. All were utilizing in addition to nitroglycerin, adjunctive forms of therapy such as low cholesterol or low fat diet, pentaerythritol tetranitrate (PETN) or various xanthine derivatives.

Within ten days maximum, and some within the first 24 hours after the institution of iproniazid therapy, all patients experienced a diminution both in the severity and the frequency of anginal seizures. All experienced a mood elevation of some degree, but none amounting to an actual euphoria. There was a distinct exercise tolerance increase, in some individuals up to a 50 per cent increase within one to two weeks.

Cesarman refers to a tendency toward normalization of the electrocardiogram. This was not observed by Cossio in his series nor in any of the series now being reported. There was no lessen-

* Roche Laboratories, Nutley, New Jersey.

ing of evidences of ischemia in any individual, but no deterioration was observed, on the other hand, with the exception of the development in one patient of a second degree A-V block occurring about one month after beginning treatment and persisting to the present writing.

Illustrative Case Histories

Case 1. H. O., a 78-year-old white woman, had severely incapacitating angina associated with hypertension. The blood pressure averaged 200/120. There was marked arcus senilis and associated cholelithiasis. Her symptoms became progressively more severe over a period of approximately 10 years. There was no antecedent history of myocardial infarction. The patient was maintained over a period of years on various forms of medical antihypertensive management with only indifferent results. She had moderate insomnia on occasion, marked emotional instability, and depression. There was electrocardiographic evidence of systolic overloading of the left ventricle.

Iproniazid 10 mg daily was begun on May 8, 1958, and was followed within approximately one week by marked decrease of nitroglycerin usage and notable elevation of mood. After approximately three months of iproniazid therapy, discontinuance of other coronary vasodilator therapy was possible with continuing adequate response and progressive lessening of both frequency and intensity of anginal seizures. No evidence was noted of iproniazid intoxication or side effects.

Case 2. G. C., a 58-year-old white man, had sustained a myocardial infarction diagnosed elsewhere in October, 1957. Since recovery, there had been marked anxiety and limitation of activity because of the occurrence of angina on exertion. He was normotensive and had moderate arteriosclerosis of the thoracic aorta. An inadequate response to PETN was noted. He complained of profound weakness particularly in the legs in the latter part of the day, but had no intermittent claudication.

Iproniazid therapy, 10 mg daily, was begun September 5, 1958. Within two days there was notable improvement in mood status, increase in exercise capacity, and diminution in requirements for nitroglycerin, in spite of elimination of PETN.

Discussion

Both Cesarman[1] and Cossio[2] appear to postulate an as yet unidentified action of iproniazid upon myocardial metabolism. Both feel that the drug offers no vasodilatory action. Cesarman notes no effect whatever upon blood pressure levels. This small series appears to corroborate Cesarman's observations. There seems as yet to be no conclusive or even impressive evidence offered to indicate that the postulate of a hitherto unknown action upon myocardial metabolites is a necessary concept. In this small series of patients, it is notable that the most striking benefits were achieved in those individuals in whom an anxiety or depressed state was a striking feature. This also was reported by Cossio, who suggests, besides, that greatest success is achieved in nonprogressive cases; this latter is not in accord with the series reported here.

One might almost feel that along with the improvement of mood and psychic habitus, the myocardial efficiency also was elevated. It is, perhaps, more appealing to think of the mechanism of operation of iproniazid in the control of anginal seizures as being mediated through the emotional structure of the patient rather than through any direct physical action. Many of these patients with a depressed outlook do very poorly, indeed, when treated with tranquilizers; the mood of depression appears to increase in many, and the anginal syndrome in these appears not notably benefited by the tranquilizer. Contrariwise, mood elevators, particularly of the amphetamine group, appear in such instances likewise to be of doubtful value. It is suggested that an increase in cardiac work may be evoked by the amphetamine drugs, offsetting possible beneficial effects derived from a mood alteration.

It appears that iproniazid can produce an improvement in emotional outlook while at the same time failing to exercise any adverse effect either on cardiac output or on blood pressure status. It is this characteristic which may well account for the apparent beneficial effects in angina pectoris of minute doses of the drug, the improvement in mood status presumably raising the threshold of the anginal syndrome in these patients, possibly through relief of some of the attendant anxiety.

Master[3] has recently reported a series of patients under therapy with iproniazid and expressed himself as being profoundly impressed with the efficacy of this treatment. It is worthy of note that he finds his most satisfactory results in those individuals in whom depression is a notable factor. Master, however, has also utilized the original dosage suggested by Cesarman and by Cossio and appears also to

have noted a considerable number of untoward side effects.

The finding of electrocardiographic changes subsequent to the institution of iproniazid therapy by Cesarman is not necessarily an argument favoring a direct somatic action of this drug; recently both Wilde[4] and Wasserburger,[5] as well as other earlier writers, have demonstrated marked effects upon the T wave and the ST segment of mood and emotional states.

Conclusions

From a small series of cases it is concluded that iproniazid is a useful medication in the therapy of angina pectoris, but that the dosage employed may be very much less than those originally recommended. In the series of patients under study, no instance of intoxication of any form has been observed over a period extending (at the time of this writing) up to approximately five months. A suggestion is advanced that the beneficial effects attributable to iproniazid may be ascribed to the effect upon the patient's psyche rather than to any direct effect upon the myocardium or the circulation thereof.

Summary

(1) Iproniazid in a dosage of 10 mg per day appears to be of benefit in the treatment of angina pectoris.

(2) No toxic effects have been noted on this dosage.

(3) It is suggested that the action of the drug may be directly upon the patient's mood status and thus indirectly upon the myocardium or the coronary circulation.

(4) It is suggested that electrocardiographic changes reported concomitant with iproniazid therapy may be explained on a psychic basis.

(5) It is suggested that iproniazid in small doses is worthy of further and more widespread trial as a therapeutic agent in angina pectoris.

Addendum

Since the completion of this paper, the author has had an opportunity to observe the effect of iproniazid in doses of 10 mg daily in an individual with continuing angina subsequent to what appeared to be myocardial infarction. The drug did not wholly relieve the discomfort, but there appeared to have been a distinct lessening of the need for narcotic drugs. It is suggested that possibly iproniazid might find a use as well during the discomfort of the early stages of myocardial infarction.

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Meprobamate in the Treatment of Angina Pectoris

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ANGINAL ATTACKS may be prevented and nitroglycerin requirements reduced not only by drugs which actively increase coronary blood flow or improve myocardial metabolism but also by agents which alter the anatomic apparatus of pain or the reaction to pain perception. Consequently, while pain may be relieved by placebos, sedatives, tranquilizers, nerve-blocking agents, and other drugs, rational therapy in angina pectoris must be aimed at the elimination not only of the cardinal symptom of the disorder but also of the underlying myocardial hypoxia which evokes it. Previous studies[1–9] employing the Master two-step test in patients with angina pectoris have demonstrated the superiority of nitroglycerin and pentaerythritol tetranitrate among more than 80 drugs assayed in this manner for prophylactic therapy in coronary insufficiency. Nevertheless, it was concluded that in patients in whom angina cannot be controlled satisfactorily by currently available vasodilators, adjuvant therapy with analgesic and tranquilizing agents may have distinct value.

The distress experienced as angina is determined not only by the intensity of the stimulus evoked by myocardial hypoxia but also by the psychic reaction to its perception. Thus, such states of feeling as anxiety, frustration, fear, and panic that may be aroused in the patient suffering an anginal attack possess the power to intensify the total experience expressed as pain. Of even greater significance, however, is the ability of these psychic states to perpetuate or augment the transient imbalance between coronary flow and myocardial requirements. Control of anxiety and tension, therefore, may minimize stimulation of the sympathetic nervous system (by catecholamines), with its associated increase in metabolism, blood pressure, and heart rate and decrease in cardiac efficiency.

The demonstrated value of meprobamate in the treatment of anxiety-tension states suggested its possible usefulness in conjunction with vasodilator drugs in the therapy of angina pectoris. In order to determine the clinical response to meprobamate, a series of patients with angina pectoris was studied by the double-blind method, employing four preparations: placebo, meprobamate, pentaerythritol tetranitrate (PETN), and pentaerythritol tetranitrate plus meprobamate.

MATERIAL

The 38 patients selected for this study all presented classical symptoms of angina pectoris which routinely responded to both the prophylactic and therapeutic administration of nitroglycerin. In every instance the diagnosis had been clearly established by the patient's history, and in more than one-third of the cases electrocardiographic confirmation of coronary disease was obtained. Eight of the 38 patients had sustained previous myocardial infarction. Thirty-one patients were male and seven female. The ages ranged from 38 to 66 years.

METHOD

(*A*) *Effect on Anginal Pain:* Each of the patients was treated with separate courses of PETN (20 mg), meprobamate (400 mg), a placebo, and meprobamate (400 mg) plus PETN (20 mg)* by the double-blind method.

* Given as 2 tablets of Equanitrate, Wyeth Laboratories. Each tablet contains 200 mg meprobamate and 10 mg PETN.

The stated dose of the respective drugs was administered four times daily, before meals and at bedtime, in successive courses of two weeks each. A record of the pain experience was kept in each instance by a notation at bedtime as to whether symptoms were the same as usual, unusually severe, exceptionally mild, or completely absent. Although 52 patients in all were studied, 14 were excluded from the final analysis because of insufficient data, poor cooperation, or unreliability of the reports.

(*B*) *Effect on Response to Exercise:* The Master two-step test was employed in 14 carefully selected patients to determine the modifying influence of the preparations under study on the electrocardiographic response to standard exercise. Each of the patients selected for this phase of the study exhibited a relatively constant positive response in control tests recorded from day to day. In addition, the control response could be favorably modified in each instance by the sublingual administration of nitroglycerin immediately preceding the test. Exercise tolerance was determined by this means in all 14 patients while receiving "blind" therapy with one of the four medications in use. A single dose of one of the preparations was administered before breakfast on consecutive mornings, 90 minutes before the performance of the test. A total of 189 tests were obtained on the 14 patients in the study. Analysis was then undertaken of the degree of ST segment depression observed in the postexercise electrocardiograms following each of the medications.

Results

(*A*) *Effect on Anginal Pain:* Evaluation of the pain experience by the "daily report card" method in 38 patients with angina of effort revealed a definite response pattern suggesting that meprobamate is more effective than placebo, and that PETN-meprobamate is more effective than PETN alone (Table I). However, since the differences cannot be regarded as statistically significant, an attempt was made to determine whether the results might be more striking in patients in whom anxiety and emotional disturbance complicated the clinical picture. Careful review of the case material indicated that 11 of the 38 patients in the series manifested nervous symptoms to a significant degree. In these 11 patients in whom anxiety symptoms were prominent, meprobamate alone or in combination with PETN appeared to reduce the frequency of pain more effectively than placebo or PETN alone, respectively (Table II). In these selected cases meprobamate appeared more effective than PETN alone but the most favorable response was consistently observed with a combination of the two agents.

(*B*) *Exercise Electrocardiographic Tests:* Careful measurement of the ST segment depression (lead V_4) immediately after exercise disclosed that the best results were obtained with a combination of PETN and meprobamate, whereas meprobamate alone and PETN alone each appeared superior to placebo (Table III).

TABLE I

Comparison of Pain Experience with Various Drugs Evaluated by "Daily Report Card" in 38 Patients with Angina Pectoris

Agent	Total no. days reported	Percentage of days in which cardiac pain was reported as			
		Same as usual	Less than usual	More than usual	None at all
Placebo	522	52.9	30.6	13.2	3.3
Meprobamate	523	53.7	34.0	9.6	2.7
PETN	522	47.7	35.8	10.0	6.5
PETN & meprobamate	523	45.3	37.1	13.8	3.8

TABLE II

Comparison of Pain Experience with Various Drugs in the Eleven Patients with Angina of Effort and Anxiety Symptoms

Agent	Total no. days reported	Percentage of days in which cardiac pain was reported as			
		Same as usual	Less than usual	More than usual	None at all
Placebo	156	51.3	32.1	15.4	1.2
Meprobamate	152	41.4	48.0	3.9	6.7
PETN	154	51.9	38.3	7.8	2.0
PETN & meprobamate	151	31.8	56.3	5.3	6.6

This pattern of response was even more clearly observed when an analysis was made of the five patients in the series who commonly experienced pain during the performance of the test following placebo therapy (see Table III).

TABLE III

Average ST Segment Depression (mm) (Lead V_4) Immediately After Standard Exercise with Various Drugs

	Placebo	Meprobamate	PETN	PETN & meprobamate
	AVERAGE DEPRESSION (mm)			
All 38 patients	1.8	1.2	1.1	0.7
5 patients with pain during tests	2.0	1.0	1.1	0.3

Discussion

In the absence of drugs which invariably prevent a critical disturbance in coronary-myocardial relationship, consideration should be given to the use of sedative and tranquilizing agents as adjuvant therapy in angina pectoris. In other disorders, analgesic agents relieve pain solely by altering the psychic reaction to pain perception while exerting little or no significant effect upon the stimulus itself. In angina pectoris, however, drugs which alter the pain threshold or modify the psychic reaction to pain perception or diminish attention to pain not only may assist in the control of symptoms but also may prevent an exaggeration of the disparity between coronary flow and myocardial requirements. Since pain in angina pectoris is a cause as well as a consequence of myocardial hypoxia, rational therapy in this disorder should be directed not only at improvement in coronary circulation and/or myocardial metabolism but also at reduction in both the severity of pain and the psychic reaction to its perception.

Although physical or emotional stress may "trigger" the anginal attack, the resultant insufficiency of the coronary circulation is in part dependent on the pain experience and the anxiety, fear, or panic to which it gives rise (Fig. 1). Such feeling states, acting through the sympathetic nervous system (catecholamines), obviously re-enforce the initiating stimulus by influencing metabolism, blood pressure, heart rate, and cardiac work and efficiency. In treating the patient with angina pectoris, therefore, it would appear logical to employ, in conjunction with the coronary vasodilator, an analgesic agent which can effectively minimize the pain experience and the psychic response which it evokes.

The findings of the present study appear to indicate that meprobamate may favorably influence the frequency and severity of anginal attacks and nitroglycerin requirements in patients with angina pectoris, particularly when anxiety symptoms are prominent. Indeed, in

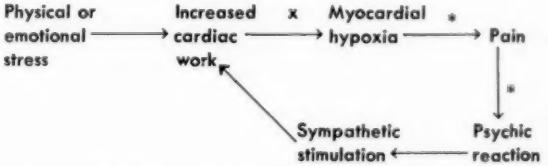

Fig. 1. Diagrammatic representation of factors involved in anginal attack. x Site of action of coronary vasodilator. * Site of action of meprobamate.

such cases, meprobamate often appeared more effective than pentaerythritol tetranitrate alone in the control of symptoms. Similarly, in patients who experienced typical angina during the performance of the Master two-step test following placebo administration, the electrocardiographic response was often as good with meprobamate as with pentaerythritol tetranitrate. The best results, however, in both clinical and electrocardiographic response, were observed with a combination of meprobamate and pentaerythritol tetranitrate in the patients studied.

Summary and Conclusions

Inasmuch as acute myocardial hypoxia associated with the anginal syndrome is significantly influenced by the psychic reaction to the perception of pain, therapy directed at minimizing the pain experience and the anxiety symptoms to which it gives rise would seem beneficial in the treatment of patients with this disorder. The demonstrated value of meprobamate (Equanil) in the treatment of anxiety-tension states suggested a trial of this drug in the treatment of patients with angina pectoris. A double-blind study, employing separate courses of placebo, pentaerythritol tetranitrate (PETN), meprobamate, and meprobamate with PETN, was undertaken in 38 patients with this disease. Using the "daily report card" method, it was found that meprobamate alone or in combination with PETN appeared to reduce the frequency and severity of pain more effectively than placebo or PETN, respectively. In patients with overt manifestations of anxiety, meprobamate often appeared more effective than PETN in the control of symptoms.

Exercise electrocardiographic tests obtained in 14 patients undergoing "blind" therapy with one of the four medications under study indicated a significantly better response to meprobamate than to placebo. The administration of pentaerythritol tetranitrate in combination with meprobamate was also followed by a distinctly more favorable response than was observed following the administration of PETN alone.

It is concluded that meprobamate is a useful adjunct in the therapy of angina pectoris. Its favorable influence in this disorder appears to be dependent on its "tranquilizing" properties rather than on coronary vasodilator action.

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Phenylindandione in Therapy of Coronary Artery Disease

Study of Its Long-term Use in Ambulatory Patients

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WITH the hope of modifying the course and prognosis of coronary and other vascular diseases by providing a satisfactory background for recanalization and the development of collateral channels, the long-term use of an anticoagulant was deemed to be logical therapy. Thus, if the common complications observed in vascular disease could be avoided by this therapy over a prolonged period of time, physiologic rehabilitation might take place with less difficulty. The anticoagulant phenylindandione* was chosen for this study because of its reputed low toxicity, its rapidity of absorption and elimination and the ease with which a therapeutic blood concentration could be maintained.[1–5] It has been shown that vitamin K_1 is an effective antagonist to this drug should complications arise from its use.[6,7] Its stability and comparatively low cost likewise added to its preference in this long-term study.

METHOD AND MATERIAL

Initial hypoprothrombinemia was induced in most of the group within 24 hours with an average dose of 300 to 500 mg, followed by a maintenance dose of from 50 to 150 mg daily. After each patient's prothrombin level was stabilized at 40 to 60 per cent of normal he reported at fortnightly intervals thereafter. A specially prepared thromboplastin extract† was used which required only the addition of distilled water for immediate use, and the technique instituted remained unchanged for the entire study.

At each subsequent examination blood and urine analysis was undertaken to determine absorption, intolerance, and dissipation of the drug. At this time each patient was clinically examined and the necessary functional and clinical studies were made and recorded.

Seventy unselected private ambulatory patients were chosen after conclusive evidence of coronary or other vascular disease was established by clinical study. A like group of patients was used as control. Each patient was observed for a period of from 2 to 7 years, an average of 3 years and 5 months in the treated group and 3 years and 7 months in the control. The anticoagulant group was made up of 58 men and 12 women with an average age of 54.7 years, while the control group consisted of 61 men and 9 women with an average of 55.6 years. All patients, treated and control, remained ambulatory throughout the period of observation and only became inactive or bedfast when recorded complications occurred.

RESULTS

Nine deaths occurred in the treated group (13 per cent) (Table I). Of these, 4 were caused by congestive heart failure and 2 by syphilitic heart disease, complicated by pneumonia in one and pulmonary embolism following hemorrhoidectomy in the other. Of the remaining deaths in this group, 1 resulted from azotemia, 1 from unquestionable myocardial infarction complicated by ventricular fibrillation and 1 from a cerebral thrombosis in

* Hedulin, Walker Laboratories, Inc., Mount Vernon, New York.
† Simplastin, Warner-Chilcott Laboratories, Morris Plains, New Jersey.

TABLE I
Analysis of Deaths in Patients with Coronary Artery Disease

Cause of death	Treated group	Control group
1. Myocardial infarction	1	19
2. Pulmonary embolism	1 (syphilis)	2
3. Congestive heart failure	4	6
4. Uremia	1	0
5. Cerebral accident	1	5
6. Pulmonary infection	1 (syphilis)	2
7. Acute left heart failure	0	2
Cause unknown	0	1
TOTAL	9	37

a patient whose prothrombin time prior to death was normal. In the control group, of the 37 patients who died (53 per cent), 19 had recurrent myocardial infarction, while in the remaining the cause of death was as diversified as in the treated group. In addition, 5 patients of this group had nonfatal myocardial infarcts.

The clinical manifestations of coronary insufficiency adequately abated in 47 of the treated group to be commensurate with normal gainful activity (Table II). Of the controls, 21 were sufficiently free from discomfort to return to productive activity, and an additional 7 were comfortable with limited activity. Among those who became active in the treated group, 12 required additional medication such as sedation or vasodilators from time to time.

TABLE II
Comparison of Clinical Findings in Treated and Control Group

	Treated group	Control group
Total patients	70	70
Number of deaths	9	37
Recurrent thrombosis or infarction	3	24[a]
Relief of cardiac symptoms	46	22
ECG improvement	41	26
Return to gainful occupation	47	21
Need for additional medications	12	28
Hemorrhagic complications	3	0

[a] 19 fatal, 5 nonfatal cases.

Among the active controls all required symptomatic drug therapy.

Hemorrhagic complications occurred in 3 patients of the anticoagulant group. In 1, it followed injury to the left knee; in the remaining 2, one developed hematuria which abated in 3 days, at which time the drug was readministered, and the other had rectal bleeding which continued for one week, requiring the cessation of the anticoagulant therapy and treatment with vitamin K_1. This hemorrhage took origin from a polyp which was subsequently cauterized and anticoagulant therapy was again instituted.

Reversal of electrocardiographic abnormalities was noted in 41 of the treated group and 26 of the controls. These changes were in keeping with the clinical improvement. In 6 of the treated group the electrocardiogram returned to normal. In general the changes occurred in the polarity of the ST and T waves, particularly in leads 1, 2, aVL, aVF, and the left-sided precordial leads. With clinical improvement, voltage increased in both groups when it was primarily subnormal and the arrhythmias were seen less frequently.

In only 2 of the 70 patients receiving phenylindandione was resistance to the drug noted. In these patients dosage of from 200 to 300 mg daily was necessary to maintain an adequate prothrombin level.

DISCUSSION

These observations are in agreement with previous studies[8–10] as to the practicability and safety of long-term anticoagulant therapy with phenylindandione. The results obtained in this group of patients appear to be even more optimistic than the results previously reported. This may be accounted for by the type of patients seen regularly in private practice, under full control of the same clinician, as compared to the average clinic or hospital patient. A study of the mortality of the treated as compared with the control patients not only reveals a lessened mortality but also infrequency of recurrent coronary accident. It appears that the use of prolonged anticoagulant therapy assists in the prolongation of life of those suffering from coronary or other vascular damage and possibly allows for recanalization or an increase in the collateral

circulation, thus reducing or abolishing the incidence of repeated coronary thrombosis and infarct.

Hemorrhagic complications in this series have been so insignificant as to allay fear. In the treated group a satisfactory and acceptable state of hypoprothrombinemia was maintained over a prolonged period of time with infrequent but regular visits by the patient. Electrocardiographic, clinical, and laboratory studies seem to support the contention that anticoagulant therapy over a long period of time assists physiologic recovery. A comparison with the control group substantiates this contention. The ability of those under therapy to receive greater subjective relief with return to a normal active environment and gainful occupation in greater numbers adds to its therapeutic usefulness. It is interesting to note that the one patient in the treated group who died of cerebral thrombosis had a normal prothrombin time prior to death. It is possible that medication may have been omitted by error.

Summary and Conclusions

(1) Phenylindandione (Hedulin) was found to be a safe and effective anticoagulant for long-term use in private ambulatory patients with coronary artery disease.

(2) The long-term hypoprothrombinemia apparently assisted the healing faculties of the body, possibly allowing for recanalization and the development of collateral vascular channels.

(3) The drug produced minimal untoward symptoms and complications, and a therapeutic prothrombin level was easily maintained.

(4) Patient morbidity and mortality rates in the treated group were lowered by its use.

(5) Complications, particularly of coronary origin such as thrombosis and myocardial infarction, were greatly reduced.

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Case Report

Melanomatosis Involving the Heart*

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METASTATIC tumors involving the heart and/or pericardium are much more frequently found than primary tumors.[1] Reports by different authors[2] totaling 8,414 (in 1951) autopsies showed an average incidence of 3.9 per cent of all tumors, including metastatic lesions, which is approximately 7.1 per cent more frequent than primary.

During the past ten years, survey of the literature on tumors of the heart, both primary and metastatic, indicates drastic changes in reports from 1930 to 1945. The recent literature implies increased frequency of both primary and metastatic lesions of the heart and/or pericardium, but this increase could be more apparent than actual. It could result from inadequate observations of the pathologist conducting the autopsy[3] and from the failure of the clinician to recognize or properly interpret significant unexplained dysfunctions occurring in the heart's activities.

In former years, the majority of cases in which the heart and/or pericardium were involved with tumors, either primary or metastatic, went undetected during life. Herbut and Maisel[4] in 1942 reported 35 cases of metastatic tumors of the heart. From 4,050 necropsies done at Jefferson Medical College Hospital, none was diagnosed ante mortem.

On the other hand, during the same era (1934–45) there were isolated cases reported in which malignancies of the heart and/or pericardium were diagnosed during the life of the patient.[5–7] There is no doubt that in the past ten years this situation has rapidly changed for several reasons, one of these being more meticulous and more frequent cell studies of serous effusions when these are present, as advocated by this author in 1934.[5] The importance of cell study was substantiated more recently by Ritz[7] and also by Piotti,[6] who reported a remarkable series of thirty cases of metastatic cardiac tumors in which the diagnoses were made in 20 of the 30 cases during life.

Yater,[8] in a magnificent contribution to the subject (1931) of cardiac tumors, states that most metastatic lesions fall in either carcinomatous or sarcomatous category, but in no way implied the infrequency of melanomatous, yet one of his nine cases reported was a case of melanosis.

Until recently, after a rather extensive review was made of the literature on metastatic melanomatosis of the heart, it was this writer's impression that such a lesion involving the heart and/or pericardium was exceedingly rare. On the other hand, after careful analysis it was determined that most of the melanomatous cardiac lesions were part of a generalized metastasis and that previous to this there was some "manipulation" of the primary tumor, possibly suggesting this "manipulation" acted as a "trigger" to the spreading of the lesion.

The increasing frequency of melanomatous encroachment of the heart is indicated by Prichard's report in 1951[1] when he reviewed 150 cases, and the breakdown revealed 102 carcinomas, 26 sarcomas, and surprisingly, 18 melanomas. The group of melanomas was not individualized

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so that it could not be determined if the metastasis of the heart was a part of generalized metastasis or if metastasis was precipitated by "manipulation" of the primary site.

The author wishes to report another case of metastatic melanoma involving the heart associated with generalized metastasis. This followed surgical removal of the primary tumor one year previous and with recurrence six months later in another area, and again surgical intervention six months prior to death.

Case History

L. H. K., age 59, readmitted to Biloxi Division, Veterans Administration Center, Sept. 5, 1957. He died Oct. 14, 1957.

In September, 1956, the patient had a large, black, flat lesion cauterized and excised from the center of the back. The diagnosis was not stated. On June 1, 1957, he had another lesion removed from the right axilla under local anesthesia. Subsequently, more cutaneous and subcutaneous nodules appeared, becoming large in size, and the patient suffered loss of appetite and general malaise.

On the last admission Sept. 5, 1957, the examination revealed a pale, fairly well nourished, white male, with evidence of recent loss in weight and looking chronically ill. Blood pressure was 124/80; temperature, 99.2; and weight 185 lb (from 220 lb formerly). No abnormal findings were noted in the heart and lungs. The liver was palpable four fingerbreadths below the costal margin with several nodules noted. Two tumors were fixed at the eighth and ninth ribs, right anterior axillary line.

Routine laboratory tests, including urinalysis, serology, and blood studies, were reported within normal range, except for simple anemia. Chest x-ray on Sept. 5, 1957 revealed several poorly defined nodular densities on the right side, varying from 1 to 2 cm in diameter, probably due to metastases.

Course in the Hospital: Following admission, the patient was treated conservatively with general supportive measures, finally resorting to narcotics for relief of pain. Later there was evidence of new metastatic lesions developing in various regions of the body accompanied by progressive physical deterioration. The patient expired quietly on Oct. 14, 1957.

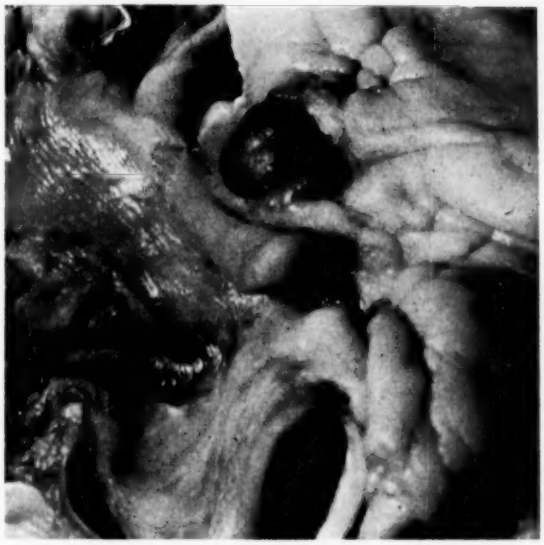

Fig. 1. Tumor mass on surface of heart and extending into wall of right atrium.

Autopsy Report

This was a 59-year-old, well developed, well nourished, white male. There was an irregular scar curved under the right arm representing right axillary radical gland dissection. Surrounding the scar there were several raised firm masses beneath the skin with an average diameter of 2 cm. In the center of the back there was a coarse oval scar, 4 × 6 cm. There were innumerable small elevated intracutaneous tumors over the skin of the entire body. There were two tumors, fixed, one in the eighth rib and the ninth rib on the anterior axillary line.

The *heart* weighed 350 g, was dark reddish-brown and rather firm. Two tumor masses, averaging 1 cm in diameter, that penetrated the wall of the left ventricle were noted. Another tumor mass, also measuring 1 cm in diameter, was present on the surface of the heart and extended into the wall of the right atrium (Fig. 1). This mass was light brown. On sectioning the heart there were noted four whitish-gray tumor masses in the wall of the myocardium of the left ventricle, averaging 1 cm in diameter. The endocardium of the left ventricle was smooth. Aortic and mitral valves were free and intact. On opening the right ventricle there was noted a

Fig. 2. Polypoid tumor mass on the endocardium of the right ventricle.

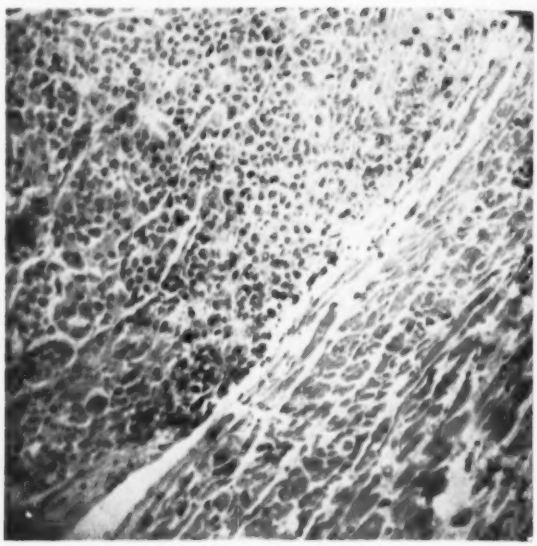

Fig. 3. Melanoma sarcoma invading and replacing the muscle tissue of the heart.

polypoid tumor mass (Fig. 2) on the endocardium of the ventricle measuring 2.5 × 1.5 cm. This tumor tissue was whitish-brown and firm. Pulmonary and tricuspid valves were free, thin, and intact. Coronary arteries were patent. There was moderate thickening of the walls of the arteries due to arteriosclerosis. The aorta revealed a few early atheromatous plaques.

The right *lung* weighed 1,000 g, the left, 1,100 g. They were purplish-gray and had a "doughy" feeling. On cut section scattered throughout both lungs were numerous small white tumor nodules that averaged 0.5 cm in diameter. Fluid exuded from the cut surfaces.

The *liver* weighed 3,500 g, was purplish-red and was enlarged. Beneath the capsule were six tumor nodules, firm and white, with an average diameter of 3 cm. On cut section throughout the liver were noted numerous whitish-gray nodules varying in diameter from 1 to 3.5 cm.

The *spleen* weighed 500 g, was purplish-gray, and beneath the capsule there was noted a whitish tumor mass measuring 3 cm in diameter, and on the cut section the mass was located in the center of the splenic tissue.

The right *adrenal gland* weighed approximately 40 g, was soft and yellow, and on the cut section this tumor tissue appeared to have infiltrated throughout the gland. The left adrenal gland was enlarged, measuring 7 × 6 cm, and on the cut section whitish-gray tumor tissue had replaced the normal adrenal tissue.

The *lymph glands* of the mediastinum were enlarged and varied in diameter from 1 to 1.25 cm. They were firm, and on the cut section had a whitish-gray color. The tumor tissue had replaced the normal lymphoid tissue.

Microscopic Examination

Sections taken through the heart revealed an anaplastic tumor which had the characteristics of melanosarcoma. This tumor was made up of oval cells with hyperchromatic nuclei invading and replacing the muscle tissue (Fig. 3). There was noted a small amount of pigment in the cytoplasm of some of the cells, and some cells had mitotic figures. A similar picture was seen in the liver, spleen, lungs, heart, mediastinal lymph glands, and the skin.

Summary

A case of metastatic melanoma of the heart is reported, adding another to the increasing number of similar cases reported in recent medical literature. This case, like the majority of others, was associated with a generalized melanosis, which in turn followed surgical manipulation of the primary lesion for one reason or another. Surgical "manipulation" of the primary lesion,

no doubt, might be imperative in many cases, and when such is the case, the most meticulous and complete dissection should be undertaken to preclude the possible hazard of general metastasis with cardiac involvement. The rapidly increasing number of cases of metastatic melanoma of the heart reported since 1951 provides a question: Should every "black mole" be removed?

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Historical Milestones

Armand Trousseau: Lecture on Angina Pectoris

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AT PRESENT it is the fashion among American teachers of medicine to belittle the lecture. Schools and scholars now speak disparagingly (and tautologically) of the so-called didactic lecture, i.e., the dogmatic or expository lecture. In order to be deemed progressive and hence superior to one's predecessors, it is necessary nowadays to expel lectures from the curriculum or to reduce their number to a fashionable minimum.

Yet the lecture has merit which will enable it to survive detraction, since a lecture well presented can transmit facts, ideas, or theories in a clear and orderly way, and at the same time can stimulate thought and arouse enthusiasm. Few contemporary textbooks show the live spirit which a good lecturer can convey to his students. Perhaps this explains why the American textbook suffers obsolescence as rapidly as the American automobile.

The excerpts which are given herewith come from the works of a great master, Armand Trousseau* (1801–67), professor at Paris and physician to the Hôtel Dieu. The reader will note the interest and diversity of the case reports as well as the clarity and accuracy of the descriptions. Details are given when necessary but the presentation is not cluttered. At the same time there are always a few special features or incidental comments which arrest the reader's attention.

EXCERPTS FROM TROUSSEAU'S LECTURE ON ANGINA PECTORIS

* * *

GENTLEMEN.—In spite of the numerous publications which treat of angina pectoris, the history of that complaint is not very satisfactorily known; and the various opinions which have been expressed as to its nature have thrown so little light on the subject that I wish, in my turn, to communicate to you my views concerning this singular neuralgia.

A woman who died some time ago in St. Bernard ward, of aneurism of the aorta, furnished us with a remarkable instance of this complaint. Her attacks, which at first occurred at pretty distant intervals, recurred very frequently toward the last, and few among you have not had an opportunity of witnessing one of those awful paroxysms.

She was suddenly seized with an excruciating pain, without any appreciable determining cause, either while sitting motionless on her bed (the only posture which she could retain) or while moving. This pain started from the precordial region, and radiated from it to the base of the chest, producing there a sensation of constriction which the patient compared to that which might be caused by an iron girdle tightened with force. It then spread to the loins, and ascending towards the cervical region, attacked

* Trousseau, A.: *Lectures on Clinical Medicine Delivered at the Hôtel Dieu, Paris.* Translated by P. Victore Bazire and John R. Cormack. New Sydenham Society, London, 1868–1872. Vol. 1, pp. 592 ff.

the left arm, and extended into the very tips of the fingers. The skin of the hand and fore-arm could be then seen to become excessively pale, and almost immediately afterwards to turn of a markedly bluish or livid tint. After the pain had ceased, the arm and hand felt numb for a few minutes. The pain was such as to make the patient cry out; her features were contracted, she sat in an upright position, as if dreading to be choked, although she breathed pretty freely. The paroxysm lasted a few seconds, and returned at intervals, which grew proportionately shorter as the disease drew to a fatal termination.

In this instance, the angina pectoris was symptomatic of an organic lesion, and such was also the case in a patient about whom I was lately consulted by Dr. Périer.

He was a military superintendent, fifty-five years old. His attacks, which dated seven years back according to his statement, were chiefly characterised by a sensation of numbness and tingling in the skin of the left axilla, and spreading from there to the whole corresponding side of the chest. He often felt shooting pain, like that of neuralgia, but which was quieted by his squeezing his back against a resisting surface, as a piece of furniture, for example.

For the last six or eight months, he had become subject to some oppression at the chest. A somewhat rapid walk, the least active exercise, brought this back, and he was troubled with pain, even if he had been engaged in merely signing away many papers, in the discharge of the duties of his post.

On examining his chest, all the physical signs of aneurism of the aorta were made out. The action of the heart was violent without abnormal bruit; higher up and in front, a distant double bellows-sound was heard, and was audible also in the back all over the left side of the chest, but in the greatest intensity along the vertebral column, on a level with the spine of the scapula. Deep percussion also over the plessimeter made out dullness over the same spot. Vesicular breathing was perfectly normal all over the chest.

These two cases would seem to confirm an opinion held by some physicians, namely, that *angina pectoris* depends on the presence of appreciable organic lesions of the heart, of the great vessels, or of neighbouring organs. You are aware that Heberden (who was the first to give to this complaint the name by which it is now known, and who has left us a pretty good description of it), and, after him, Parry, Kreysing, Burns, J. Frank, &c. ascribed angina pectoris to ossification of the coronary arteries. Others, on the contrary, have referred it to hypertrophy with dilatation of the heart, ossification of the auriculo-ventricular or aortic valves, pericarditis, accumulation of fat on this membrane in the mediastinum or on the heart itself, displacement of this organ, compression of it by a tumor or through abnormal development of some one of the abdominal viscera, aneurismal dilatation of the aorta, inflammation of this vessel, mediastinal abscess, ossification of the costal cartilages, &c.

I do not deny that angina pectoris may coexist with one or other of these various lesions, and that it often (most often, perhaps) is symptomatic, as has been said, of organic diseases of the heart or of the great vessels. But while, on the one hand, the variety of these lesions makes one suspect their etiological value, on the other, the numerous cases in which such lesions exist without the patient suffering from anything like paroxysms of angina pectoris, and, per contra, authentic instances of individuals who during life presented all the characteristic symptoms of angina pectoris, while, after death, dissection disclosed no anatomical lesion by which these symptoms could be accounted for, prove that this complaint is not essentially due to the presence of organic disease.

From the absence of appreciable structural changes, and from the extreme variability of the phenomena, which I shall endeavour to describe to you, we must conclude that angina pectoris is a neurosis, or to use a more precise term, a neuralgia. As to its seat, which some have placed in the diaphragm, others in the respiratory muscles, and most in the heart, this neuralgia generally affects the cardiac nerves given off by the pneumogastric, and radiates to the nerves of the cervical and brachial plexuses.

One of my oldest and most intimate patients, a lady, forty-seven years old, suffered in her youth from very obstinate chlorosis, accompanied by very acute neuralgic pain, which varied much in

its seat. For some years past, she has had very mobile rheumatoid pains, attacking sometimes the limbs, and at other times the viscera, and curious nervous disorders, which might be called hypochondriasis, if this lady were not a person of very great sense. I may add that her health is excellent, as far as the functions of organic life are concerned. For the last two years, she has noticed that, when she goes up a staircase pretty quickly, she is suddenly seized with an acute pain behind the sternum, rapidly extending to the left shoulder and arm, and causing trifling numbness. On her stopping, the sensations disappear in less than a minute. I have examined her heart and her lungs with the greatest care, I might say, with the most devoted solicitude, on several occasions, immediately after she just had one of these seizures, and never at any time have I discovered in the heart's rhythm, in the valvular sounds in the region of the aorta, or in the lungs, the least sign, the least phenomenon, different from what is found in health, with the exception of some marked acceleration of the heart's action.

Quite recently, when I intended to speak to you of angina pectoris, I was consulted by a gentleman, aged forty-five, who had all the appearances of the most flourishing health. He took more than ten minutes to come up to my door, and, when in the ante-room, he dropped on a bench, looking pale, and in a condition which frightened my servant. A few minutes sufficed to make him right again.

When, half an hour afterwards, he came into my consulting room, I could never have suspected from his blooming appearance what had so lately occurred. He then told me that fifteen years ago he had had a very bad attack of syphilis, of which he had not been well cured. Three years afterwards, he had a very violent and obstinate attack of sciatica, and, subsequently, pains in the limbs, of which he was cured, after many unsuccessful treatments, by iodide of potassium. Later again, he had had an attack of gout in the big toe. He had never passed any gravel, and there was no history of gout in his family antecedents.

The angina pectoris had begun a year previously. The attack was very slight, and only recurred when he took any violent exercise, at rare intervals; in a short time, less active causes sufficed to bring on a paroxysm, which recurred at more frequent intervals. For some months, for the last month particularly, his life had become unbearable. If he happened to walk up the least ascent, he was instantly seized with pain, and was compelled to stop. He had just come from Lyons on the day when he consulted me. He had travelled all night, and as he came out of the railway carriage, he had to walk a few steps about the station to get a cab. Although he walked quietly, he was seized so violently that he had a kind of fainting fit, and was obliged to sit down in the mud. His travelling companions put him upon his legs again. The pain which he felt was excruciating; it began behind the sternum, nearly on a level with the fourth and fifth ribs, somewhat about the region of the heart, which beat violently during the attack. It extended from there to the root of the neck, and to both arms equally, causing a painful sensation of numbness as far as the tips of his fingers. He fancied that his hands swelled a little at such times. He was then obliged to stop short, and to keep his chest motionless, dreading to draw in his breath lest he should increase the fearful constriction which crushed his chest. When the pain was more intense, he was seized with vertigo, and fell into a state almost like syncope.

The emotion which my examination caused him, and the movements which he made to take off, and afterwards put on, his clothes, sufficed to bring on a slight paroxysm.

It would certainly be difficult to meet with a more marked case; and I confess that I felt sure I would find some grave lesion of the heart, or of the great vessels. But on the most searching examination, I detected no abnormal condition of the intra-thoracic organs. And as I have already met with a good many cases of this kind in the course of my career, and as I have seen persons as gravely affected as this gentleman was get perfectly well, I must of necessity admit that angina pectoris, even when most intense, need not be a symptom of an organic lesion. . . .

A case, however, recently came under my notice and that of my esteemed friend, Dr. Marx, which shows that one should be very careful before affirming that no organic lesions

exist. An ex-bill-broker on the Paris Bourse, who had been formerly subject to very severe hepatic colic, which had left him for several years, began to complain of choking sensations which came on suddenly whenever he took a little more active exercise than usual. The sensation of choking was accompanied by an acute pain behind the sternum, radiating to the left shoulder and arm. There was no habitual dyspnoea, and nothing could excite the suspicion that the *angina pectoris* was a symptom of an organic lesion. But auscultation afterwards detected the presence of an aneurism of the arch of the aorta which increased rapidly, and from that time, there came on habitual orthopnoea, and paroxysms of angina pectoris recurred on the patient making the slightest movement. Dr. Marx had one day spent a few moments with him, encouraging and consoling him, and had been accompanied by him on his going away as far as the bedroom door; but the doctor had no sooner got to the bottom of the stairs than he was hastily summoned by the patient's servant. On going up again in all haste, he found a corpse. The aneurism had suddenly burst into the trachea, and had caused fatal haemoptysis.

In the month of September 1865, I was consulted by a patient sent to me by Dr. Lefebvre of Roubaix, and suffering from angina pectoris. The complaint had set in suddenly about the middle of the preceding year, during an after-dinner walk, and the paroxysms had recurred several days in succession. They disappeared for some time, and then returned with greater intensity than ever, *at the same hour* invariably. They soon ceased from being periodic, and recurred under the influence of the slightest effort, or during sleep, on the patient starting up. At last, symptoms of a serious hypertrophy of the heart, with lesions of the ventricles, showed themselves. I will, therefore, willingly admit that, in some cases, even though the most careful examination will not be able to detect anything in the aorta or in the mediastinum, there are lesions present which become manifest at a later period. . . .

When I first began practice, I attended for several years a gentleman whose complaint I did not for a long time recognise, and whose case taught me a lesson which I have never forgotten. He was sixty years of age, and enjoyed excellent health. Two of his brothers had died of a sudden death, and in one of them the cause was found to be rupture of an aneurism.

For some years past, this gentleman complained of a violent pain about the base of his chest, in the course of the intercostal nerves; the pain was most intense in front, and where it was so, the skin was also slightly benumbed. It sometimes left the chest, and spread to the sides of the neck and head, where it simulated a neuralgia.

The symptoms were not constant, but returned at uncertain intervals. All the medical men whom the patient had consulted, and I among the rest, thought that the case was one of rheumatic neuralgia. After a few years, the pain became almost continuous, although it was very bearable. When the patient tried to walk, however, it became so fearfully intensified that he was compelled to remain almost motionless. Rest made everything right, as is the case in angina pectoris; but he often could find no relief except by lying flat on his stomach on a couch. He tried I know not how many plans of treatment. His great wealth allowed him to consult the most eminent practitioners, and to spend two or three months every year at various mineral springs. At last, he complained to me one day of a queer throbbing sensation in the back, on a level with the seventh and eighth ribs on the left side. On laying my hand over that part, I felt an impulse isochronous with the heart's beat. From that time, percussion and auscultation settled all doubt about the existence of aneurism of the aorta. The disease made rapid progress; four ribs became eroded after a time, and a tumor of the size of a child's head showed itself under the skin. I need not add that the case terminated as such cases always do; the aneurism destroyed the skin, and burst suddenly outside. . . .

The frequently perfect periodicity presented by neuralgias due to some grave organic lesion is something very remarkable. I have already related to you the cases of two ladies suffering from carcinoma of the uterus whom I saw with Récamier and with my excellent friend, Dr.

Lasègue. In 1862, I saw a third case of the kind, that of a lady with a uterine polypus, whom I attended with Professor Nélaton. In all three the most fearful neuralgic pain recurred every day at the same time, with the regularity of the most typical ague.

Some of you may also remember a man who was at No. 10, in St. Agnes ward, and who suffered from pains returning every day at the same time, with unspeakable violence, sometimes accompanied with an attack of unilateral eclampsia, after which there remained some hemiplegia. After death, we found cancer of the brain.

I lay so much stress on the perfectly periodic character of neuralgias, due to the gravest organic lesions, because some pathologists have asserted that periodicity, when well marked, was a character distinguishing pure neuroses from neuralgias depending on a grave organic visceral lesion.

In the case of angina pectoris, the periodic recurrence of the attacks by no means, therefore, excludes the idea of an organic affection of the heart, or its valves, or of the great vessels. I admit, and the majority of practitioners do so, that this singular neurosis may be symptomatic; but I admit it merely in this sense, namely, that there is a mere coincidence, and that the organic lesions, whatever they may be only afford an opportunity for the development of the neurosis which is superadded to them.

I merely advert now to the fact that neurosis may be engrafted on organic lesions, and be independent of them since those lesions are persistent, and cannot, therefore, be regarded as the essential condition and the true cause of nervous disturbances which are of a transient character.

Some patients state that sudden atmospheric changes bring on the paroxysms, or that they cannot walk, run, or ride, against the wind without being compelled to stop from an attack of the complaint.

The most frequent causes, especially when the angina pectoris is due to an organic lesion of the heart or of the great vessels, are sudden movements, unusually active exercise, as brisk walking, or the act of going up a staircase, or, again, fits of coughing, prolonged speaking, straining at stool. These efforts or these muscular movements need not even be very violent, since, as in the case of the military superintendent whose history I related to you in the beginning of this lecture, the pain came on after the patient had been engaged in putting his signature to many papers.

In some instances, the first seizures come on after some excess in eating or drinking; in many cases the paroxysms are always more violent after a meal, even when moderate, whether the individual moves about or remains quiet. Jurine has, however, recorded the case of a man whose attacks were most violent and prolonged when he was fasting.

Deep mental emotions, especially fits of anger, are frequent exciting causes of angina pectoris, and they not only bring on a paroxysm, but they increase the intensity of the disease to such a degree as even to cause death.

Such are the circumstances in which the singular affection which has engaged our attention today comes on in the majority of instances, although no rule can be laid down concerning it. Their multiplicity shows the essentially nervous nature of the complaint, and this fact will become still more evident from the changeableness of the symptoms.

It almost never happens that angina pectoris is ushered in by premonitory symptoms: its access is sudden. Pain is suddenly felt behind the sternum, accompanied with a sense of constriction and anxiety, generally seated in the left side of the chest, but occasionally in the right side, and it is so intense as to make the patient dread suffocation and syncope, and to deprive him of the power of speech.

It is rarely confined to that part, for in nearly every instance it spreads simultaneously, sometimes along the neck as far as the articulation of the lower jaw, the movements of which are impeded, but more frequently along the pectorales muscles to the shoulder-joint, from which it descends along the inner aspect of the arm as far as the elbow, and down the fore-arm to the fingers.

The left side is the one generally attacked, as I have told you, but in some cases the right is the side affected, as in the epileptic patient whose history I have related to you. In other

cases, instead of ascending to the neck or arm, the pain descends to the epigastrium as far as the groin; in others, again, but very rarely, it is felt in all those regions at the same time.

Its extension to the upper extremity is so constant a phenomenon that some authors, particularly Wall, who described angina pectoris nearly simultaneously with Heberden, have given it as an essential character of the disease.

It has occasionally been known to follow an opposite course, beginning in the arm, and thence quickly spreading to the chest. Do you not find, gentlemen, great analogy between this and what occurs in the *aura epileptica*, and is not this in contradiction to the view that angina pectoris is of necessity caused by a material lesion of the organs contained in the thoracic cavity.

Sometimes, again, this pain is felt in the hand alone, without starting from the chest, and without passing along the nerves of the arm, or taking an ascending course.

On March 29, 1863, I saw, in consultation with Drs. Gruby and Maître, a Russian nobleman suffering from hypertrophy of the heart with systolic bellows-murmur at the apex. He felt from time to time an acute pain in the cardiac region, which disappeared after having been strictly local; then all of a sudden, without any manifestation about the heart, he had in the left hand a pain which he compared to that of cramp, and which was accompanied with numbness. There was no muscular spasm. The pain lasted about a minute, and disappeared without leaving any traces.

Lastly, in some cases, angina pectoris consists in violent palpitation, with numbness of the left arm, without pain. This was the case in a young married lady, aged twenty-two, who consulted me on November 22, 1862. Her grandfather had been gouty, her mother suffered from violent neuralgias, and she herself had been subject to angina pectoris since she was sixteen years old. For the space of four years, she had only had excessively violent palpitation, without any sensation in the arm, but for the last four years the palpitation was accompanied by painless numbness of the left arm, which compelled her to drop whatever she might be holding in her hand. These symptoms recurred whenever she took a little more active exercise than usual. I found no signs of cardiac or valvular lesions.

When pain is present, as unquestionably happens in the great majority of cases, it is not generally increased by making pressure over the affected parts, or by moving the arm into which it extends. Nay, mere pressure may relieve it, and I may again remind you on this point of the patient, whose history I have already related to you, and who used to relieve his throbbing pain by squeezing his back against a piece of furniture.

Although patients suffering from angina pectoris think they are going to be suffocated during a paroxysm, the chest is normally resonant on percussion, and if it be auscultated as they draw in breath again, vesicular breathing is heard everywhere. This is far from being the case in fits of dyspnoea.

Should the patient assume any peculiar attitude, it is on account of the pain, and not from distress of breathing. Very varied attitudes are assumed: one patient will lie motionless on his back; another will incline backwards on the back of his chair, or on his pillows; a third will place himself on all fours, resting on his knees and elbows; while a fourth may stoop so much as to bend in two. . . .

The extreme variability of the phenomena which characterise angina pectoris often render its *diagnosis* very uncertain, and it is not surprising that very different conditions have been confounded with it. As Wichmann remarked, twenty-five years after Heberden, an individual need only complain of anxiety, and of a sense of constriction about the chest, even of impeded breathing, for its being immediately ascribed to angina pectoris.

Thus, pleurodynia of the praecordial region, which set in suddenly, and temporarily impeded respiration, disappearing rapidly, has been mistaken for angina pectoris. The pain, in such cases, is more superficial than that of angina pectoris, and does not, like it, shoot beyond the part which it attacked in the first instance. It is seated in the pectorales muscles, and is relieved and even removed by taking in a deep breath, prolonged for a while, and by

making pressure on the affected part. Lastly, it is not lancinating, and is not accompanied by a sense of anxiety, and is not followed by a feeling of numbness like angina pectoris.

The diagnosis is made with difficulty when an individual afflicted with aneurysm of the aorta suffers from sternal pains, shooting toward the shoulder, and accompanied by a sense of choking which, from its growing worse at times, might lead one into error. But, even then, these pains do not recur in very distinct paroxysms; they are continuous, or at least, never cease spontaneously. The same remark applies to the pungent, lancinating, and excruciating pain, attended with oppression at the chest, which occasionally supervenes in pericarditis.

In conclusion, in spite of their extreme diversity, the characters of angina pectoris are such that it seems to me difficult to mistake them.

As a rule, I know nothing so difficult as the treatment of nervous disorders. Neuroses are not only capricious in respect of their etiological conditions and of their symptomatic manifestations, but of their amenability to treatment also. Some patients get well after the use of remedies which fail in others, and a treatment which has proved unsuccessful in one case is sometimes followed by the best results in instances apparently perfectly similar. The very variability of their manifestations, the suddenness of their invasion without any appreciable cause, and their oft-unexpected abrupt cessation frequently throw doubt on the real utility of our interference. This is especially the case in angina pectoris. The paroxysms are often of such short duration, and generally terminate so suddenly, that their disappearance can hardly be ascribed to the influence of treatment. If they have been brought on by somewhat active exercise, as a brisk walk, or by running, the patient need only stop still to cause the phenomena to pass off, although cases have been recorded in which individuals have, in defiance of the pain they felt, continued to walk, and have got rid of it. Some persons have been able to stop the paroxysm by forcibly holding their breath. . . .

On the hypothesis, admitted by some, as I have told you, that angina pectoris is due to ossification of the coronary arteries, *phosphoric acid* has been recommended, with the view of preventing and even of removing these ossifications. I need not add that this absurd idea could only occur to a chemist, who should have studied physiology and medicine before dabbling in therapeutics. . . .

* * *

Comments

As these selections demonstrate, Trousseau's *dramatis personae* is as varied as that of Balzac. Russian noblemen, military superintendents, brokers on the Bourse, all were included in his variegated clientele. These patients and other anonymous gentlemen and ladies furnished a variety of dramatic statements and impressive incidents. The unfortunate woman who suffered from aneurysm compared her angina to "an iron girdle tightened with force". A forty-five-year-old man had paroxysms which terrified the doctor's servant. The broker had an aneurysm which burst into the trachea.

The finer clinical portrayals are no less noteworthy. Thus, in the first case, one of aortic aneurysm, the successive alterations of color and sensation in the left arm are described with great care. The various typical and atypical radiations of pain are also set forth in several instances.

In discussing the mechanism of angina pectoris Trousseau lists the lesions which have been found by various observers. Their diversity points to the extensiveness of the anatomical observations which had accumulated by this time but it also points to the lack of a general hypothesis broad enough to account for all the facts. Trousseau clearly says that the variety of the lesions encountered makes one suspect their etiological value, especially since in some cases no lesions whatever were encountered. He concluded that angina pectoris was a neuralgia which was usually engrafted on an organic disease of the heart or vessels but which might also occur independently.

Diagnostic Shelf

Austin Flint Murmur vs. Mitral Stenosis

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A 57-year-old colored widow was admitted to the hospital with a two-year history of increasing exertional dyspnea and paroxysmal nocturnal dyspnea. The patient knew that she had contracted syphilis 15 years before and thought that a complete cure had been obtained with 12 injections of bismuth. The patient had been informed that she had high blood pressure in 1947, but she did not receive any treatment. This history was otherwise noncontributory.

PHYSICAL EXAMINATION

The patient was a well-developed and well-nourished female with no orthopnea. The peripheral pulses were full and bouncing. The pulse was 100 and regular, and the blood pressure was 180/90. There were no thrills. The apical thrust was not visible or palpable; the apex was percussed below the 6th rib at the axillary line. The right cardiac border was percussed 2 cm outside the margin of the sternum. Palpation revealed a prominent pulsation below the lower part of the sternum. There was a soft, blowing diastolic murmur in decrescendo over the entire precordium, louder over the aortic area. Other findings were: a faint systolic murmur over the aortic area, a diastolic-presystolic rumble at the apex, 2nd sound accentuated and "tambour-like" over the aortic area, and 1st sound accentuated at the apex. The liver was palpable one finger below the right costal margin. The jugular veins were not engorged, but there was a positive hepatojugular reflux.

LABORATORY TESTS

The *chest x-ray* with barium swallow showed a diffuse enlargement of the heart, an aneurysmal dilatation of the ascending aorta, minimal displacement of the esophagus by the aortic arch, and a moderately enlarged left atrium. The *electrocardiogram* showed moderate left axis deviation, left ventricular hypertrophy and strain, and normal P waves and P-R interval. The first sound occurred 0.09 sec after the Q wave of the ECG.

PHONOCARDIOGRAM

The tracing reveals the absence of an opening snap and of gallop sounds, and gives the evidence of an early-diastolic murmur at the base and a presystolic murmur at the midprecordium and apex (Fig. 1).

Various studies made on the blood and urine were not contributory and are not reported for brevity. The various serologic reactions for syphilis were negative.

Discussion

At this point of the study, the general interpretation of the case was that the patient had syphilitic heart disease with aortitis, aneurysm of the ascending aorta, and aortic insufficiency. Problems which were not solved were the following: (1) Has the patient also rheumatic heart disease; if so, has she mitral stenosis? (2) Has the patient atherosclerosis of the aorta, causing some degree of obstructing aortic stenosis? (3) If not, has the patient only an Austin Flint murmur?

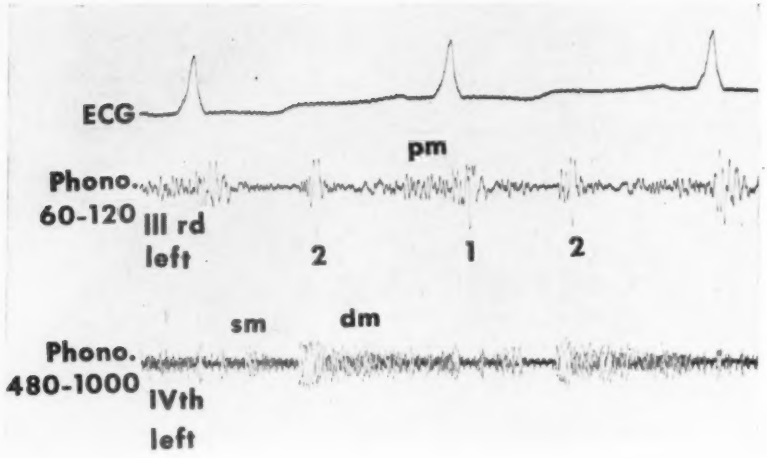

Fig. 1 Phonocardiograms with two different degrees of filtration, showing the apical presystolic rumble (above) and the transmitted basal, blowing diastolic murmur. *pm* = presystolic murmur; *sm* = systolic murmur; *dm* = early-diastolic murmur.

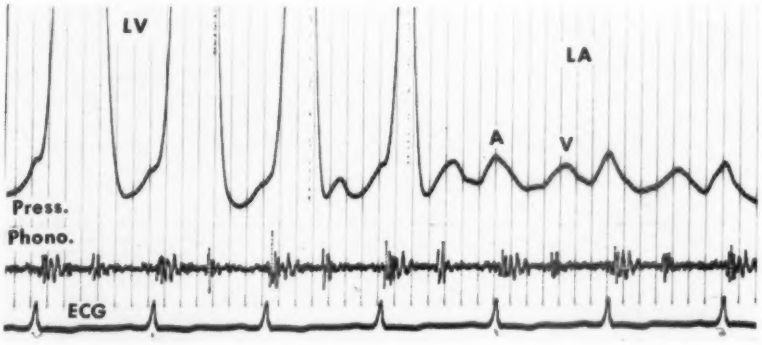

Fig. 2 Left heart catheterization. Pullback from LV to LA; no diastolic gradient across the mitral valve.

For the above reasons, it was decided to perform a *left heart catheterization.* This revealed the following data: (1) no evidence of aortic stenosis, as indicated by the lack of any systolic gradient between left ventricle and aorta; (2) no mitral stenosis, as indicated by the lack of any diastolic gradient between left ventricle and left atrium (Fig. 2); and (3) no evidence of mitral insufficiency, as indicated by the preservation of the normal pattern in the left atrial pressure curve (Fig. 2). (4) Intracardiac phonocardiography revealed a minimal systolic murmur within the left atrium and a moderate diastolic murmur within the left ventricle.

In conclusion, it was felt that the diastolic-presystolic murmur was an Austin Flint murmur, caused by eddies which formed within the dilated left ventricle, and that there was a moderate left ventricular failure (diastolic pressure within the left ventricle was from 5 to 20 mm Hg).

In retrospect, it is apparent that many data were against the existence of mitral stenosis (in addition to aortic insufficiency), such as the lack of an opening snap and of a split 2nd sound, the lack of abnormalities of the P waves, and the lack of evidence of right ventricular hypertrophy in the electrocardiogram. The enlargement of the right heart was logically due to failure. The prolongation of the Q-I interval, once considered specific for mitral stenosis, is now interpreted as being nonspecific and frequently found in hypertension or other conditions in which left ventricular hypertrophy occurs. The fact that the diastolic pressure, measured at the arm, was not too low could be explained by the combination of left ventricular failure and systemic hypertension. The pulse pressure was actually still much larger than normal. The high level of diastolic pressure in the left ventricle is partly explained by the regurgitant jet from the aorta and partly by left ventricular failure. The patient was digitalized and advised to receive a course of penicillin injections. She went home improved.

Progress Notes in Cardiology

Edited by EMANUEL GOLDBERGER, M.D., F.A.C.C.

New York, New York

Pulmonary Embolism and Infarction

IN AN experimental study of pulmonary embolism and infarction, Drs. Brent M. Parker and John R. Smith (Washington University School of Medicine, St. Louis) found that a dog's lungs, embolized with pieces of rubber catheter did not develop pulmonary infarction unless femoral arteriovenous fistulae were created. It was felt that the A-V communications diverted blood from the collateral circulation of the lungs (the bronchial arteries). As a result the blood supply was not adequate to prevent pulmonary necrosis when the pulmonary artery was occluded. Experimental studies have rather consistently demonstrated that embolized dog lungs do not develop pulmonary infarcts unless the normal circulation is impaired. These studies correlate well with clinical observations that infarction does not follow embolism unless congestive heart failure is present, although definite infarcts do occasionally occur in otherwise healthy patients.

In a review article in the *American Journal of Medicine* (24: 402, 1958), these authors attempted a physiologic explanation of the events of pulmonary embolism and infarction. Some conclusions that seemed justified on the basis of the literature were: (1) Pulmonary thromboembolism is greatly underdiagnosed. (2) From 50 to 60 per cent of patients with pulmonary emboli develop lung infarcts. (3) The condition is more frequent on medical than on surgical wards. (4) Both phlebothrombosis and thrombophlebitis are potential sources of pulmonary emboli.

The literature concerning pulmonary embolism and infarction has nearly always considered the two conditions together, without an attempt to differentiate their symptomatology. Although an exact differentiation is impossible, and symptoms may merge, some separation can be made. Characteristic manifestations of pulmonary embolism are dyspnea; substernal, oppressive chest pain; manifestations of cerebral ischemia (restlessness, syncope); electrocardiographic changes; shock; right-sided heart failure; and sudden death. If pulmonary infarction develops as a consequence of pulmonary embolism, the patient may develop pleuritic chest pain, hemoptysis, cough, dyspnea, fever, elevated leukocyte count, and densities on chest x-ray examination.

Unusual features of pulmonary vascular accidents, suggesting the proper diagnosis, may include unexplained fever not responding to chemotherapy, increase in the severity of congestive heart failure, paroxysmal arrhythmias, or unexplained bloody pleural effusion.

Treatment of Intractable Ascites by Bilateral Adrenalectomy

SEVERE ascites in patients with cirrhosis is usually associated with extreme urinary sodium retention. Since aldosterone may be necessary for such degrees of sodium retention, and since aldosterone output is known to be very high in these patients, bilateral adrenalectomy appears to be a rational form of treatment for those patients in whom conventional forms of treatment have failed. Drs. Keith S. Henley, David H. P. Streeten, and H. Marvin

Pollard (University of Michigan) describe a cirrhotic patient on whom bilateral adrenalectomy was done.

The patient previously had been incapacitated for five years with intractable ascites, resistant to a strict 200 mg sodium diet and to various diuretic agents. Seventeen days after the operation, when the dosage of hydrocortisone had been reduced to maintenance amounts, the patient went into negative sodium balance. In the subsequent 31 days, the ascites and peripheral edema disappeared completely, weight fell by 8.2 kg, and exchangeable body sodium declined from 5,200 to 2,050 meq. A striking improvement in appetite, muscular strength, and sense of well-being coincided with the loss of ascites. She has been observed for 10 months since the operation, and is asymptomatic and leading virtually a normal life.

They conclude that the presence of adrenal salt-retaining corticoids was essential for the persistence of ascites in this patient, and that removal of the adrenals was an effective and beneficial form of treatment. However, in the present state of our knowledge, adrenalectomy should be reserved for patients without severe hepatocellular damage who continue to gain weight on a 200 mg sodium diet and who fail to respond to the usual diuretic measures.

The Query Corner

READERS are invited to submit queries on all aspects of cardiovascular diseases. Insofar as possible these will be answered in this column by competent authorities. The replies will not necessarily represent the opinions of the American College of Cardiology, the JOURNAL or any medical organization or group, unless stated. Anonymous communications and queries on postcards will not be answered. Every letter must contain the writer's name and address, but these will not be published.

Digitalis in Heart Block

Query: A 65-year-old patient who had 3:1 A-V heart block of ten days' duration developed signs of congestive heart failure and was digitalized with 2.5 mg digoxin in 36 hours. He promptly developed Stokes-Adams attacks due to ventricular asystole which recurred for several days and ended fatally. Was this related to the digitalis therapy?

Answer: Probably not, although one cannot be sure. Digoxin might be blamed for deterioration of the partial A-V block to complete, but not for failure of a ventricular pacemaker, or for persistence of complete block for several days after the drug had been discontinued. The choice of a rapidly dissipated glucoside was wise; the drug was administered cautiously, as is advised in cases of partial block with congestive failure. The short duration of the 3:1 block prior to the onset of Stokes-Adams attacks suggests that worsening of the degree of block was due to progression of disease rather than to an effect of the drug.

Failure of the ventricular pacemaker in this case is not surprising, since for 3:1 A-V block to occur at all one must assume a low order or rhythmiticity in the A-V node or bundle of His. With an atrial rate of 75, for example, the ventricular rate with a 3:1 block would be only 25; ordinarily under such a circumstance an idioventricular pacemaker would "take over."

If the block was related to acute or subacute infarction in the ventricular septum it might have been lessened or abolished by the use of an adrenal corticoid.

EDGAR HULL, M.D.
New Orleans, Louisiana

Sublingual Heparin Therapy

Query: What is the present status of sublingual heparin therapy for hypercholesteremia?

Answer: About 5 or 6 years ago, using anticoagulant techniques, no absorption of heparin could be demonstrated when administered orally, sublingually, or rectally. However, there have been recent reports of the clarification of postprandial lipemia (but no anticoagulant activity) following sublingual heparin. In view of the physiologic role of heparin in fat transports, and its use in the control of atherosclerosis, the advent of orally effective heparin would be significant. In these reports, however, only serum optical density changes were measured, and no determinations made of triglyceride lipolysis or removal of fat from the bloodstream. Parenteral heparin, even when injected in a small dose, results in the production of an active fat-splitting enzyme, rapid disappearance of chylomicra and low-density beta lipoproteins, and loss of fat from the blood.

Unfortunately, more thorough investigation has not indicated that sublingual heparin is absorbed in the majority of individuals when the actual amount of lipemia-clearing factor or the concentration of heparin in the blood was determined. A fat-splitting enzyme was demonstrated in the blood in only 3 of 21 normal subjects after the buccal or sublingual administration of an oral heparin (Clarin). In some of the same subjects 2 mg of heparin intravenously uniformly produced an excellent lipemia-clearing factor response and increased heparin levels.

The explanation of the discrepancy in results

is not quite clear but may reside in the fact that a deceptive, nonlipolytic clearing occurs, as with gastric mucin. The oral heparin, which is not highly purified, may well contain other mucopolysaccharides which cause decreases in optical density but do not remove fat from the blood. In any event, since sublingual heparin was absorbed in only 3 of 21 individuals, it should not replace parenteral heparin in the therapy of atherosclerosis.

H. Engelberg, M.D.
Beverly Hills, California

Coarctation of the Aorta

Query: A 45-year-old woman with coarctation of the aorta and aortic stenosis has severe angina pectoris both at rest and on exertion. Should surgery be performed, and if so, which lesion should be tackled? What are the operative risks in a patient of this age?

Answer: There might well be many individual features of this case which would influence a decision one way or the other. However, we must assume that no such pertinent factors exist. One, therefore, is faced with a 45-year-old (young?) patient who almost certainly is suffering from significant aortic coarctation and congenital (noncalcific) aortic valvular stenosis. There is a strong probability that the aortic valve will be found to be of bicuspid formation and, hence, not completely restorable to an ideal normal.

While the patient presents evidence of severe coronary insufficiency, this must be considered as functional (due to the valvular dysfunction and the arterial hypertension associated with the coarctation) rather than intrinsic, since organic coronary arterial disease is rare in uncastrated women of this age.

It is the writer's opinion that the chief circulatory impediment in the presumably average case presenting this picture would be attributable to the valvular stenosis. Therefore, the valvular obstruction first should be relieved by direct-vision aortic commissurotomy, using hypothermia or (preferably) the aid of a heart-lung by-pass. At a later date the coarctation might be corrected electively.

The operative risk in a properly managed patient with this problem should be of the order of 20 per cent, largely because of the unavoidable retention of a portion of the excess ventricular load (that part attributable to the coarctation) during and after the operative relief of the valvular obstruction.

Charles P. Bailey, M.D.
Philadelphia, Pennsylvania

Book Reviews

Lehrbuch der Roentgenologischen Differentialdiagnostik: Vol. I. Diseases of the Chest, ed. 4, by Werner Teschendorf. Georg Thieme Verlag, Stuttgart, 1958 (Intercontinental Medical Book Corporation, New York), pp. 1183, illus. $50.00.

About half of this volume dealing with the heart and great vessels, the mediastinum, pulmonary circulation, and diseases of the pleura is of immediate concern to the internist with a main interest in cardiology.

P. Thurn, author of the section on the heart proper, had at his disposal the ample clinical material of the medical and surgical clinics of Bonn and Düsseldorf, and also the cineroentgenographic material of Robert Janker, Bonn.

While the presentation presupposes some average roentgenologic knowledge, the newer, more complicated methods, such as electrokymography and cardiac catheterization, are very well described in technical details of practical performance. The general presentation is fluent, with references to the numerous illustrations. These, mostly roentgenograms, but also electrokymographic and other tracings, photographs of specimens, etc., are well chosen and reproduced with extraordinary clarity; they all have concise yet ample legends. The reading and refinding of passages are substantially aided by page headings and numerous marginal subtitles, from one to three or four on some pages, a feature used by the author already in his first edition in 1937. The bibliography is amazingly up to date (to late 1957), comprising German, French, British, the latter comprising about 50 per cent of the entries, and in some chapters even more. They are placed at the bottom of each page.

In the discussion of the roentgenologic methods in general application the reviewer has been impressed by the wide use of kymography, both classical roentgenkymography and electrokymography with the phase analysis of Heckmann, which, despite a promising start, is hardly used in this country at present. A roentgenographic by-product of heart catheterization is the determination of the volume of the right heart chambers. Angiocardiographic findings are interspersed for elucidation of individual problems but do not contribute an essential part of the roentgen diagnostic effort as presented here.

The differential diagnosis of pulmonary roentgen findings can be oriented according to the size, shape, density, and arrangement of the "shadows." The roentgen findings in cardiology are quite unmanageable for such an arrangement. Thus, the diagnostic effort is centered about the normal roentgen anatomy and the understanding of the hemodynamic disturbances. In close application of Zdansky's teachings the distinction of resistance overload and volume overload is amply discussed, and the pathophysiology and roentgenologic manifestation of their isolated occurrence, combination with each other, and association with myogenic insufficiency are elaborated. Then, in traditional fashion, the discussion of dilatation of the individual heart chambers is followed by the presentation of clinicopathologic entities. The discussion of measurement of the heart size in exact figures is held in agreement with the general modern attitude which accords to those measurements a very modest place in everyday practice.

The chapters on congenital heart disease, arranged according to R. Bing's classification, make ample use of diagrams and of illustrations from catheterization, kymography, and angiocardiography. The presentation is clear and here as well as in other chapters the limitations of roentgen diagnosis are well drawn; e.g., mitral valve lesions can be diagnosed with amazing accuracy in more than 95 per cent of clinically symptomatic cases. However, it is refreshing to read a frank statement that in numerous individual instances the distinction between mitral stenosis and insufficiency, or a combination of both, and furthermore the association of mitral with aortic valve lesion cannot be made as to their elements.

The remainder of the volume deals with the

pathology and differential diagnosis of the diseases of the lung, pleura, esophagus, and diaphragm. It is a rich mine of information for every diagnostic radiologist and roentgenologically interested internist and thoracic surgeon, equally as systematic study material, source of reference, and helpful guide for teaching. Not only text and pictorial material are of the highest quality, but this book as a whole represents an outstanding publishing accomplishment. FELIX G. FLEISCHNER, M.D.

Cardiac Arrest and Resuscitation, by Hugh E. Stephenson. C. V. Mosby Company, St. Louis, 1958, pp. 378, $12.00.

In the preface the author states: "Ineffectual resuscitation is still appallingly frequent. From our observations we believe that almost every physician loses his first case of cardiac arrest. This situation is deplorable. It is for this reason that a book devoted in its entirety to the problems of sudden cardiorespiratory failure and subsequent resuscitative procedures has been written. . . . Through the cooperative efforts of physicians the world over, the author has been able to establish The Cardiac Arrest Registry. . . . Many of the conclusions presented herein are based on a study of over 1,700 cases of cardiac arrest from this registry as well as from work done in the experimental laboratory over the past several years. A most comprehensive bibliography has been collected at great effort during the past eight years. . . . Nearly all physicians will be confronted with the challenging opportunity to resuscitate the acutely arrested heart. Effort must be expended to see that success at these moments is assured."

The scope of this book is indicated by the titles of chapters and the number of pages devoted to each subject: History (15 pp.); Incidence (20 pp.); Diagnosis (6 pp.); Etiology (64 pp.); Management (74 pp.); Pitfalls, Precautions, Complications (26 pp.); Prognosis (6 pp.); Prevention (20 pp.); Cardiac Arrest and Open Heart Operations (10 pp.); Care of Patient After Resuscitation (7 pp.); Neurological Sequelae (6 pp.); Bibliography (52 pp.). It is obvious that this book contains a large amount of material. It is well written, it has good balance, and it is an excellent reference book. This was the primary purpose of the author, and he has succeeded in bringing together almost everything that relates to this subject. This book, therefore, is highly recommended.

Emphasis upon completeness of coverage of literature also carries with it the possibility of weakness from dilution. It is more difficult to learn how to resuscitate the heart from 371 pages than it is from 10 pages. The presentation of method by the author lacks the emphasis that should be applied to those steps that are right and condemnation of those steps that are wrong. The person doing resuscitation wants to know these steps without equivocation. The author fails to divide the resuscitation procedure into two parts. The first part concerns restoration of the oxygen system, which is the emergency act, and the second concerns restoration of the heart beat, which is not an emergency act. This reviewer has had considerable teaching experience in resuscitation and believes this separation is nothing less than essential for understanding the procedure. This separation is a guide for doing the right thing at the right time and for not doing the wrong thing which takes precious moments of time.

Our experience with the external defibrillator is that it stops fibrillation in the dog, and when it is applied within 70 sec from the onset of fibrillation a coordinated contraction usually occurs. When it is applied after 70 sec there is no contraction, and this absence of heart action is failure. Experience with the pacemaker is that it is effective in the Stokes-Adams syndrome and it may be useful in heart block following operations inside the heart. Our experience in dogs, even when the pacemaker is applied directly on the heart, is that it is of no value after the heart stops beating in standstill or fibrillation. Both of these instruments are condemned in resuscitation because their use takes time which should be spent on restoration of the oxygen system. Almost the same thoughts are expressed by the author: "It seems likely that in the near future a satisfactory method for closed chest defibrillation will eventually be worked out. Here again, however, the problem of knowing exactly what the heart is doing makes the open chest maneuver continue to assume a great deal of importance. Unless one knows the exact status of the heart in cardiac arrest—that is, whether it is fibrillating or in plain asystole—then time spent using the closed chest defibrillation method or the closed chest pacemaker apparatus is all but wasted." The statement that time spent with the closed chest pacemaker is all

but wasted conveys a correct thought, but the impact should be that its use may cost a life and is, therefore, condemned. This is more than a difference in style of writing. It is conviction concerning right steps and wrong steps. If the right steps are known then we must have conviction concerning their value so that precisely these steps will be taken.

This book is a storehouse of interesting information. It will occupy an important place not only in resuscitation but also in the broad field of medical literature. It is a good book for your library. CLAUDE S. BECK, M.D.

Heart Disease and Pregnancy: Physiology and Management, by C. Sidney Burwell and James Metcalfe. Little, Brown & Company, Boston, 1958, pp. 338, $10.00.

Recent physiologic and clinical studies, such as those reported by the authors of this important book, have increased tremendously our knowledge and understanding of the effects of pregnancy on the heart and circulation of the normal and cardiac pregnant woman. This excellent book is an outgrowth of their studies carried out in the Boston Lying-In Hospital over a six-year period and reflects their tremendous personal experience in this aspect of cardiology.

Discussed in great detail are the incidence, prognosis, and management of the various types of cardiovascular lesions seen in pregnant women and the specific problems related thereto. Although all the common conditions are well covered, special attention is paid to rheumatic heart disease, which is the most common and important cardiac lesion encountered in pregnancy. The indications for therapeutic interruption of pregnancy are reviewed in the light of the improved prognosis of the pregnant cardiac patient. One aspect which is still unsettled and controversial is the question of mitral valve surgery during pregnancy. Despite the increasing number of reported successful commissurotomies during pregnancy, Burwell and Metcalfe still "would recommend for valvotomy only those pregnant women who suffer intractable failure before the fourth month of pregnancy on the best medical regimen. . . ." Their conservative attitude is based on the premise that surgery does not eliminate the danger to both mother and fetus consequent to disabling mitral stenosis. The reviewer's experience so far coincides closely with that of the authors.

This is a well-written and organized book on an important subject and will be read with great profit by all physicians who deal with the pregnant woman with heart disease. S. D.

Drugs: Their Nature, Action and Use, by Harry Beckman. W. B. Saunders Company, Philadelphia, 1958, pp. 728, $15.00.

This new textbook in pharmacology is modern, well organized, and written in a style which reflects the felicity of diction of the author. Recent advances, new concepts, and many important new drugs are included. Generic and trade names are given.

The book is divided into three parts:

Part I delineates the role and reward of the pharmacologist. It orients the student regarding the relationship of pharmacology to the other basic medical sciences.

Part II discusses the nature of drugs, their source, action, and fate in the body, as well as important clinical effects.

Part III discusses the actions and clinical applications of drugs. In this section pharmacology is the chief subject matter and the basic principles and fundamental mechanisms of action are treated in a comprehensive manner. The descriptions are clear and completely adequate for the needs of the medical student. Selected references for further reading appear at the end of each chapter.

Dr. Beckman's book adequately reflects his broad experience as a teacher of pharmacology and his skill as a medical writer.

JOHN C. KRANTZ, JR., M.D.

College News

AMERICAN COLLEGE OF CARDIOLOGY

Eighth Annual Meeting

MAY 25–29, 1959

Benjamin Franklin Hotel, Philadelphia, Pennsylvania

Registration and Meeting of the Board of Trustees will take place on Monday night, May 25

Scientific Program

First Scientific Session

Tuesday, May 26, 9:00–10:30 a.m.

Symposium on

NEW ADVANCES IN THE RADIOLOGIC DIAGNOSIS OF HEART DISEASE

Moderator: ROBERT P. GLOVER, M.D., F.A.C.C., Philadelphia, Pa.

1. Image Intensification in Relation to the Diagnosis of Congenital Heart Disease.
   JOHN A. KIRKPATRICK, JR., M.D., Philadelphia
2. The Use of Gas and Opaque Contrast Media in the Radiologic Diagnosis of Heart and Pericardial Lesions.
   HERBERT M. STAUFFER, M.D., Philadelphia
3. Direct Intracardiac and Great Vessel Opacification Studies.
   J. STAUFFER LEHMAN, M.D., Philadelphia

Second Scientific Session

Tuesday, May 26, 1959, 2:00–5:30 p.m.

Symposium on

BIOPATHOPHYSIOLOGY OF ARTERIOSCLEROSIS

Moderator: E. GREY DIMOND, M.D., F.A.C.C. Kansas City, Kan.

1. Pathogenesis.
   AARON KELLNER, M.D., New York
2. Biochemistry.
   DON FREDRICKSON, M.D., Bethesda
3. Coagulation and Fibrinolysis.
   TAGE ASTRUP, M.D., Copenhagen
4. Epidemiology and Genetics.
   ANCEL KEYS, M.D., Minneapolis
5. Other Aspects of Treatment.
   DAVID ADLERSBERG, M.D., New York
6. Hormonal Factors.
   HOWARD A. EDER, M.D., New York

Fireside Conferences

Tuesday evening, May 26

1. Postmyocardial Infarction Syndrome.
   WILLIAM DRESSLER, M.D., and WILLIAM LIKOFF, M.D., F.A.C.C.
2. Effect of Heart Disease on Pulmonary Function.
   GEORGE R. MENEELY, M.D., F.A.C.C., and DAN LUKAS, M.D.
3. Myocardial Metabolism.
   RICHARD J. BING, M.D., F.A.C.C., and RICHARD GORLIN, M.D., F.A.C.C.
4. Role of Fibrinolysis in Heart Disease.
   TAGE ASTRUP, M.D., and EUGENE E. CLIFFTON, M.D.

5. Indications and End Results for Surgery of Aortic Disease.
   ROBERT P. GLOVER, M.D., F.A.C.C., and DWIGHT E. HARKEN, M.D., F.A.C.C.
6. Electrolyte Balance in Congestive Failure.
   HUGH E. LUCKEY, M.D.
7. Subendocardial Infarction.
   MYRON PRINZMETAL, M.D., F.A.C.C.
8. Chlorothiazide and Analogues.
   JOHN H. MOYER, M.D., F.A.C.C.
9. Surgery of Coronary Heart Disease.
   CHARLES P. BAILEY, M.D., F.A.C.C., and DAVID S. LEIGHNINGER, M.D., F.A.C.C.
10. Art and Science of Digitalization.

Third Scientific Session

Wednesday, May 27, 9:00 a.m.–Noon

Papers by College Members.

Fourth Scientific Session

Wednesday, May 27, 2:00–3:30 p.m.

Symposium on
SPACE MEDICINE

Moderator: ASHTON GRAYBIEL, M.D., F.A.C.C.
Pensacola, Fla.

Annual Business Meeting

Wednesday, May 27, 4:00–5:30 p.m.

Groedel Memorial Lecture on Humanities in Medicine

Wednesday evening, May 27

The History of Coronary Disease.
PAUL KLEMPERER, M.D., New York

Fifth Scientific Session

Thursday, May 28, 1959, 9:00–Noon

Symposium on
THE USE AND ABUSE OF CARDIAC BYPASS

Moderator: J. MAXWELL CHAMBERLAIN, M.D., F.A.C.C., New York
IVAN D. BARONOFSKY, M.D., New York
DANIEL F. DOWNING, M.D., F.A.C.C., Philadelphia
DONALD B. EFFLER, M.D., Cleveland
CONRAD R. LAM, M.D., Detroit
HENRY SWAN, M.D., Denver

Annual Guest Lecture

Thursday, May 28, 2:00–3:00 p.m.

Role of Fibrinolysis in Cardiovascular Disease.
TAGE ASTRUP, M.D., Copenhagen

Sixth Scientific Session

Thursday, May 28, 3:30–5:30 p.m.

Symposium on
MANAGEMENT OF COMPLICATIONS ATTENDANT TO CARDIAC SURGERY

Moderator: OSLER A. ABBOTT, M.D., F.A.C.C.
Emory, Ga.

Seventh Scientific Session

Friday, May 29, 9:00–11:00 a.m.

A. *Symposium on*
NEWER ADVANCES IN CLINICAL AUSCULTATION OF THE HEART

Moderator: W. PROCTOR HARVEY, M.D.
Washington, D.C.

Friday, May 29, 11:00 a.m.–Noon

B. *Symposium on*
RECORDING AND INTERPRETATION OF CARDIAC SOUND

Moderator: ALDO A. LUISADA, M.D., F.A.C.C.
Chicago

1. Objective Proof of Functional Rumbles Simulating Mitral Stenosis (Autopsy, Right and Left Heart Catheterization, Intracardiac Phonocardiography).
   ALDO A. LUISADA, M.D., F.A.C.C.
   Chicago
2. Studies of Ultra-Low Frequency Precordial Movements (Kinetocardiograms).
   E. E. EDDLEMAN, JR., M.D., Birmingham, Ala.
3. Low Frequency Tracings of Precordial Displacement and Acceleration.
   LESLIE M. ROSA, M.D., Chicago

Eighth Scientific Session

Friday, May 29, 2:00-3:30 p.m.

Symposium on
PRESENT AND FUTURE OF
CINEANGIOCARDIOGRAPHY

Moderator: ISRAEL STEINBERG, M.D., New York

1. Angiocardiography.
   ISRAEL STEINBERG, M.D., New York
2. Biplane Cineangiocardiography with 11-Inch Image Intensifiers.
   HERBERT L. ABRAMS, M.D., San Francisco
3. Technique.
   F. MASON SONES, JR., M.D., Cleveland
4. Cyanotic Congenital Heart Disease.
   JOHN A. CAMPBELL, M.D., Indianapolis
5. Acquired Heart Disease (Noncongenital).
   J. GERARD MUDD, M.D., St. Louis

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